pp. 887-982] November, 1944

TROPICAL DISEASES BULLETIN

VOL. 41.] 1944. [No. 11.

MAIN CONTENTS :

	PAGES
Medical Organization and Diseases of Indo-China ...	887–898
Summary of Recent Abstracts IX.—Leprosy	899–904
Rabies...	904–914
Malaria	914–926
Blackwater Fever	926–927
Trypanosomiasis	928–929
Leishmaniasis...	930–931
Fevers of the Typhus Group...	931–936
Yellow Fever	936–937
Dengue and Sandfly Fever ...	937–939
Plague...	939–940
Bacillary Dysentery	940–941
Amoebiasis and Intestinal Protozoal Infections ...	941
Relapsing Fever and other Spirochaetoses	942–945
Helminthiasis...	945–959
Deficiency Diseases	959–960
Haematology	961
Venoms and Antivenenes ...	961–962
Dermatology and Fungous Diseases	962–965
Miscellaneous...	965–976
Book Reviews	977–982

For detailed Contents see pp. ii, iv, vi and vii.

Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1.
(Telephone: MUSEUM 5041)

[Price 2/6 Net. *Entered as Second Class Matter in the U.S.A. Post.* [Annual Subscription 21/-

HONORARY MANAGING COMMITTEE

APPOINTED BY THE SECRETARY OF STATE FOR THE COLONIES.

Chairman : A. G. H. Smart, *C.M.G., M.B.E.*, M.D., D.P.H., D.T.M. & H. (*Chief Medical Adviser to the Secretary of State for the Colonies*).

Wm. Horner Andrews, D.Sc., M.R.C.V.S.

Major-General Sir Ernest W. C. Bradfield, *K.C.I.E.*, I.M.S. (retd.).

Sir Wilson Jameson, *K.C.B.*, LL.D., M.D., F.R.C.P. (*representing the Ministry of Health*).

Professor Patrick A. Buxton, M.A., M.R.C.S., L.R.C.P., D.T.M. & H., F.R.S. (*representing the Royal Society*).

Sir Philip Manson-Bahr, *C.M.G., D.S.O.*, M.D., F.R.C.P., D.T.M. & H.

Sir Edward Mellanby, *K.C.B.*, M.D., F.R.C.P., F.R.S., K.H.P. (*representing the Medical Research Council*).

E. R. A. Merewether, M.D., M.R.C.P., F.R.S.E., K.H.P.

Brigadier G. S. Parkinson, *D.S.O.*, M.R.C.S., L.R.C.P., D.P.H., R.A.M.C.

J. B. Sidebotham (*of the Colonial Office*).

Secretary: C. A. Grossmith, *of the Colonial Office*.

STAFF OF THE BUREAU:

Acting Director: Charles Wilcocks, M.D., M.R.C.P., D.T.M. & H.

Acting Assistant Director: J. F. Corson, *O.B.E.*, M.D., D.P.H., D.T.M. & H.

Secretary: R. L. Sheppard.

LIST OF ABSTRACTERS IN THIS ISSUE.

D. J. Bauer, M.B., B.Chir., Ph.D.

T. Bedford, D.Sc., Ph.D.

J. F. Corson, *O.B.E.*, M.D., D.P.H., D.T.M. & H.

J. D. Fulton, M.A., B.Sc., Ph.D., M.B. Ch.B., D.T.M.

I. A. Galloway, D.Sc., M.R.C.V.S.

Professor R. M. Gordon, O.B.E., M.D., Sc.D., F.R.C.P., D.P.H.

Lt. Col. W. F. Harvey, *C.I.E.*, M.B., F.R.C.P.E., D.P.H., I.M.S. (retd.) (*Sectional Editor*).

F. Hawking, D.M., D.T.M.

Professor Edward Hindle, M.A., Sc.D., Ph.D., F.R.S. (*Sectional Editor*).

C. A. Hoare, D.Sc.

W. S. S. Ladell, M.R.C.S., L.R.C.P.

G. Lapage, M.D., M.Sc.

Maj.-Gen. Sir John W. D. Megaw, *K.C.I.E.*, D.Sc., M.B., B.Ch., I.M.S. (retd.) (*Sectional Editor*).

Sir H. Harold Scott, *K.C.M.G.*, M.D., F.R.C.P., D.P.H., D.T.M. & H.

P. G. Shute, F.R.E.S.

H. M. Sinclair, D.M.

H. S. Stannus, Ph.D., M.D., F.R.C.P., D.T.M. & H. (*Sectional Editor*).

H. W. Swann, M.B., B.S. Kieff.

Sydney Thomson, M.D., F.R.C.P., F.R.S.E. (*Sectional Editor*).

Miss Janet Vaughan, D.M., F.R.C.P.

C. M. Wenyon, *C.M.G., C.B.E.*, M.B., B.S., B.Sc., F.R.S. (*Sectional Editor*).

F. Norman White, *C.I.E.*, M.D., D.P.H., I.M.S. (retd.) (*Sectional Editor*).

V. B. Wigglesworth, M.D., B.Ch., F.R.S.

Charles Wilcocks, M.D., M.R.C.P., D.T.M. & H

BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 41.] 1944. [No. 11.

MEDICAL ORGANIZATION AND DISEASES OF INDO-CHINA

BEFORE THE JAPANESE INVASION

By Charles WILCOCKS, M.D., M.R.C.P., D.T.M. & H.,

Acting Director, Bureau of Hygiene and Tropical Diseases.

MEDICAL ORGANIZATION.

The head of the medical services of Indo-China is the Inspector General of Public Health, under whose direction are the Provincial Health Officers and their subordinate staffs. In general, except in some of the larger centres, there is no distinction between Medical Officers concerned only with curative medicine, and Health Officers concerned only with sanitation. It is thought that the native mind is not yet sufficiently educated to grasp the difference, that the native expects any doctor to treat any disease, and that he would not understand or have confidence in a medical man who was concerned only with public health. The policy adopted by the French, therefore, has been to make medical officers responsible for the purely public health aspects of medical work in addition to hospital practice.

The annual medical budget amounts to about 10 per cent. of total expenditure.

There are about 110 European medical men actually at their posts at any one time, not including the teaching staff of the medical school of Hanoi, and 240 native medical practitioners, principally Annamites, who have received their training locally. Subordinate staff comprises hospital assistants, dispensers, nurses and midwives ; of the last there were 331 in 1927. There are over 450 medical institutions, including European and native hospitals, infectious diseases hospitals, maternity institutions, dispensaries and leper asylums. It is noted that in Cochin-China during 1921 about one-third of all childbirths took place in maternity hospitals or were attended by qualified persons.

In addition to work in stationary institutions, monthly tours of rural areas are conducted by the sick-attendants. The object of these tours is not so much to give treatment to all the sick, as to detect the cases and to direct them to the treatment centres. Preventive duties include vaccination against smallpox and cholera, antimalarial

measures, treatment of venereal disease and the spread of medical knowledge. Medical education is also part of the school curriculum, and emphasis is laid on mothercraft and domestic economy.

Higher medical education is well organized. At Hanoi there is a medical school at which native doctors are trained. The course occupies four years, and some of the students pass after graduation to medical schools in Paris. Nurses and midwives are trained at Cholon, dispensers at Hanoi.

There are two Pasteur institutes, one at Saigon and one, concerned largely with veterinary medicine, at Nhatrang in Annam. These institutes provide vaccines for several diseases, and there are, in addition, vaccine institutes and public health laboratories at Hanoi, Hué and Pnom-Penh. Smallpox lymph is prepared at Hanoi and at a vaccine farm in Laos.

Quarantine stations have been established at Haiphong, Tourane, Nhabé, Saigon, Pnom-Penh. At these centres the usual arrangements are made to inspect immigrants and to hold them in quarantine if suspected of infective disease. Clayton apparatus for the fumigation of ships and river craft is available at several places. The public health service includes, however, not only these stationary institutions, but also mobile units which, though employed in connexion with matters of general hygiene and sanitation and with vaccination against epidemic diseases such as smallpox and cholera, pay particular attention to the serious problem of trachoma. In Laos the health organization is still very imperfect, but in recent years there has been a development in the use of aircraft for public health purposes. There is considerable movement of Annamite labour into Laos for the construction of roads and other works. To cope with this migration from the point of view of the introduction of infective disease, several observation posts have been established on the labour routes.

Insect-Borne Diseases.

Malaria.—Over the greater part of the country it is probably safe to assume that every indigenous native suffers from malaria not once only, but many times during his life. It is not possible to give any accurate account of the number of people who suffer actual attacks during any one year, since the majority of these persons, as is inevitable in any country in which the strength of the medical staff is relatively low, are not seen by doctors who can carry out the examination necessary for accurate diagnosis, but there are available figures of those treated in hospitals for the disease, which may be set against the total treated for all sicknesses. From these returns it was found that in 1937 malaria accounted for one-fifth of all hospital cases—from 15·7 per cent. in Tonking to 28 per cent. in Laos—and it is known that in medical institutions it causes, in general, more deaths than any other disease except cholera.

The distribution of malaria in Indo-China is not even, and it provides a good illustration of the fact that low-lying swampy ground is not always the most dangerous. Careful surveys of the country have been made by the French authorities, and the results of these have shown that malaria is most prevalent in the foothills and mountainous districts of the whole country, and in the high plateaux of the south, and is least prevalent (though still present) in the great deltas of the Mekong and the Red River.

The explanation of this fact is to be found in the biological habits of the mosquitoes which carry the disease. Some species of *Anopheles* prefer swamp water, others cannot breed unless the water is brackish, others demand the small backwaters of mountain streams open to the sun, others must have shade and relatively cool water. Further, the adult *Anopheles* mosquitoes vary in their feeding habits: some prefer human blood, and these are therefore the most dangerous, others will seek out animals and for this reason, if cattle or pigs or horses are at hand, are less likely themselves to be infected even if for any reason driven to attack man. In the absence of animals, however, these mosquitoes will feed on man.

Thus, in the delta of the Red River round Hanoi are found *Anopheles vagus* and *Anopheles hyrcanus* var. *sinensis*, both of which breed in swamps, irrigation canals or rice fields, but which are strongly attracted to animals: malaria is not very prevalent in this region. The same holds good of the delta of the Mekong near Saigon. In the hills and foothills, however, breeding conditions in the streams, especially in the dry season when they are not torrents, are favourable to *Anopheles minimus*, *Anopheles jeyporiensis* and *Anopheles maculatus*, all of which are attracted to man and all of which are dangerous vectors of malaria, probably for that reason.*

This matter is stressed here because of its importance to the health and efficiency of the natives of the country and also because of its bearing on the health of labourers and especially of those imported into malarious districts, of whom, if they have not acquired an immunity to the disease by constant infection, malaria takes a heavy toll. Subtertian malaria is found abundantly in Indo-China. The less common quartan malaria is relatively mild and its distribution is patchy. The geographical distribution of the three forms of malaria within Indo-China is not uniform; the reason for this is not clear, but the fact is of considerable importance. Thus, for instance, in the delta of the Red River and the low-lying country around Saigon, benign tertian malaria is the type most commonly found, though subtertian may occur in seasonal epidemics. In the highlands of Cochin-China, the mountains and high plateaux of Annam, the wooded mountains of Cambodia, the highlands of Laos and Tonking, and on the vast calcareous spurs of the latter, subtertian malaria is predominant and widespread. Blackwater fever is seen especially in the mountains of Annam and Tonking.

The effect of subtertian malaria on the population inhabiting these highly infected regions may be devastating. The children become infected in early infancy, and in the absence of quinine or other specific treatment, there is a high infant mortality. Even if the infants escape death they pass through long periods of ill health, with recurring bouts of fever and consequent emaciation which is superficially concealed by the protuberance of the abdomen caused by the enormous enlargement of the spleen due to the disease. In districts in which the malaria is transmitted throughout the year, immunity is acquired during childhood and youth, and adult life is passed in a state of chronic infection which, however, is compatible with reasonably good health. If the disease is transmitted seasonally, by reason of the seasonal increase of

* This is not a complete list of the *Anopheles* of Indo-China. In addition *A. aconitus*, *A. tesselatus*, *A. barbirostris*, *A. philippinensis* and others are found, but they are of less importance.

mosquito breeding due to climatic conditions, the immunity acquired is to some extent lost in the periods of non-transmission. The result is that in adult life the natives suffer from the disease year after year, and may be liable to blackwater fever. This peculiarity in the natural history of malaria is of very great importance in industry. There have been considerable movements of native labourers from areas where malaria is not common, into plantations in these districts of high incidence, and the result has been a high degree of disease, and consequent loss of time and fall in production, and, where measures have not been taken to ensure adequate treatment, a high death rate from the disease.

Preventive measures include the siting of labour and other camps away from mosquito breeding places, the elimination of breeding by drainage, by the clearing and periodic flushing of streams, by regulation of shade, by the covering of water with oil or Paris green, and by means of drug administration to the labourers. With anti-malarial drugs the French authorities in Indo-China claim highly successful results, but drug prophylaxis (suppressive treatment) is usually combined with the other measures. It is most important that these matters be borne in mind if there is any question of movement of population or of troops.

Dengue.—This is a mosquito-borne disease of little intrinsic importance which should, however, be borne in mind by medical men in Indo-China. The vector is the mosquito *Aëdes aegypti*, which breeds in domestic collections of water and which readily attacks man. This mosquito is the common carrier of yellow fever in the countries in which that disease is found, so that if yellow fever were introduced into Indo-China, there is every reason to believe that it would spread widely. With the development of air travel it is possible that infected mosquitoes or persons in the incubation (and infective) stage of the disease may be transported from Africa to India and the Far East, to initiate epidemics in those countries. The measures in force in India and other countries, to prevent the introduction of yellow fever, are well known to health authorities; to be effective the whole-hearted support of the administrative services is necessary.

Plague.—There are said to be three permanent foci of plague in Indo-China, at Cholan, Pnom-Penh and in Kwang-Chow-Wan (Tsché-Kam and Tang-Hai) respectively. The first is small, the other two of greater importance; all are in the Chinese communities of the places concerned.

Plague has also from time to time been introduced from abroad, from Canton and Hong Kong, and has spread from one part of the country to another, for instance from Cochin-China to Annam. Plague is closely associated with grain stores and with ships and ports, in all of which rats find suitable harbourage, and it is largely spread along commercial routes. The most dangerous rat is the black rat, *Rattus rattus*, because it frequents human habitations, and the most efficient flea vector is *Xenopsylla cheopis*.

The common form of the disease is bubonic, but there have been recorded from the island of Kassutin in the Mekong, and from Vinh-Long in Cochin-China, outbreaks of the fatal pneumonic form.

Plague has occurred in all the countries of Indo-China, the places particularly mentioned being Tourane, Haiphong, Lang-Son, Bac-Ninh and Hongay. In 1914 there were 2,054 cases with 1,587 deaths, but in recent years the incidence has been less and it is not now regarded as a serious problem, though its reintroduction from abroad is clearly

always possible. Antiplague vaccination has been performed on a considerable scale and anti-rat measures have been applied in the permanent foci.

Typhus.—Three forms of typhus are found in Indo-China. The classical, epidemic, louse-borne type has been seen repeatedly in Tonking, and outbreaks have occurred in the Hanoi gaol, recalling significantly the name gaol fever applied to the disease in Europe in past years. Movements of refugees may provide conditions suitable to an outbreak, but in fact, large epidemics have not been recorded. The second form is that which is essentially a disease of rats and which is conveyed to man by rat fleas. It has been found in the rats of Saigon, Hanoi, Nam-Dinh and Tuyen Quang, and in man repeatedly in Cochin-China, in Hué, where in 1931 it was noted that the disease was relatively benign, and in railway coolies in Annam in 1908. The third, mite-borne, type, a form probably identical with scrub typhus of Malaya, mite fever of Sumatra, and tsutsugamushi disease, has been reported from Cochin-China, especially in European prospectors, from Annam, where it is frequent in the Mois, and from Cambodia, where 20 cases were recorded in plantation labourers in 1937. It is transmitted to man by larval mites found in scrub or bush country, and may be expected in considerable amount in troops or labourers operating in such country.

Relapsing Fever.—This disease has been recorded in Cochin-China and Annam recently, but has not been seen in epidemic proportions for many years. In the early part of the century, however, epidemics did occur, but treatment with salvarsan brought them under control. In Indo-China this disease is conveyed by lice, which are universal, and is especially prevalent, as is typhus, under conditions of over-population and poverty.

Nutrition.

The state of nutrition of the agricultural classes of Indo-China is poor. For half the year the diet available for these people is just adequate in quantity though poor in quality, but during the other half they exist on almost a starvation level. In general, they know little food other than rice taken with salt or preserve. Other classes fare better; vegetables, fish and meat are eaten in Cochin-China, Cambodia and S. Annam, more rarely in Tonking and N. Annam. Fish is commoner than meat, and freshwater fish, sea fish and shellfish are used. The commonest meat is pork, and pigs are extensively bred; dogs are also used as food and buffalo meat is eaten, poultry are frequently kept and their eggs eaten. Besides rice, the staple food, certain other crops are cultivated: maize is relatively widely grown, the soya bean is encouraged, and with its rich protein and fat content is a valuable addition to the diet. From it are prepared soya milk and soya cheese. In addition manioc, yams, taro, sweet potatoes, beans, cucumber, China cabbage, sesame seeds, sugar cane and a number of vegetables are grown. Of the fruits the banana, lemon, pineapple and shaddock, are most common, but the orange, Chinese potato, pawpaw, bread fruit, coconut and mango are cultivated. This is a considerable list, and the wealthier classes and the people in the districts where these foods are available obtain an adequate diet, but the fact remains that a vast proportion of the 22,000,000 inhabitants exists on a diet of rice which in quantity is barely adequate.

Much polished rice is used in Indo-China, but fortunately, the common native method of milling rice is not so complete as the mechanical

method, so that some part of the vitamin-containing layers of the grain is left. Nevertheless, according to one authority, 3,000 to 4,000 cases of beriberi are diagnosed each year and ten per cent. of these patients die of the disease, which ranks eighth in the list of diseases treated in hospitals. For the year 1937 the incidence figure of 25,706 cases is given in another report, with 250 deaths. It is noted that the distribution of the disease is wide, but that in Laos and Kwang-Chow-Wan it is not so prevalent, since polished rice is not much used. In Cochin-China, where the use of polished rice is increasing, there are many grave cases, especially between the ages of 20 and 45, in women after childbirth, and in coolies. Treatment with vitamin B_1 gives excellent results.

There is a report to the effect that stone in the bladder is a common condition in young children. This may be evidence of vitamin deficiency and in India has been associated particularly with lack of vitamin A.

Water Supplies.

The question of water supplies is closely bound up with disease in tropical countries. Not only do water-borne diseases occur in epidemic form, but water is essential for the breeding of the mosquito vectors of malaria, filariasis, dengue and, in countries where it occurs, yellow fever. In general, the rainfall in Indo-China is plentiful, but as rice is one of the staple crops, irrigation is used, and entails the construction of canals, which provide a difficult problem in anti-malaria work and, since the natives use this water for drinking purposes, in the control of water-borne disease.

The domestic water supplies in the large cities are good, they are carefully supervised and are distributed over piped systems; there is therefore little difficulty in cities like Hanoi and Saigon and almost all provincial capitals. The sources of these city supplies are usually deep wells, but in Hué and Pnom-Penh river water, after full treatment, is used. At Haiphong the local water is brackish and the city supply is therefore obtained from the river 35 kilometres distant.

In the larger rural centres high level reservoirs, pumping stations and distributing systems are being installed, and water is obtained from rivers, malaria drainage systems and other sources. Small purifying plants are gradually being introduced. In the course of time these measures may be expected to be highly successful, and to exert a definitely beneficial effect upon public health, but the matter is not everywhere so straightforward. In the delta of the Mekong and the Donnai the land is almost at sea level and is traversed by innumerable canals and watercourses which are largely affected by the tides. The water is therefore brackish, and the line of demarcation between fresh and brackish water in these watercourses varies with the periods of the year. For drinking purposes, therefore, rain water is largely used, and the natives have formed the habit of conserving water in ponds. Surface ponds must, under these conditions, inevitably be heavily contaminated. There is a considerable trade in water, and water sellers, whose methods cannot be satisfactory, are common.

In the more remote rural districts where the supply is obtained from shallow wells, unprotected streams or canals, contamination is general. Such supplies are used indiscriminately for all purposes—for the watering of animals, the washing of clothes and for drinking, and although, fortunately, tea made with boiling (and therefore sterile) water is a

common drink, enough water is taken in the raw state to afford some part of the explanation of the heavy incidence of cholera, typhoid and dysentery.

Intestinal Diseases.

Cholera.—Cholera has appeared in epidemic form in Indo-China many times since the beginning of the century, but French medical writers claim that it has usually been introduced from other countries and that it is not merely a question of an endemic disease flaring up periodically to epidemic proportions. Thus, in 1926, cholera was introduced from India by way of Siam, and produced the great epidemic which affected the whole of the Far East. In 1937 the influx of refugees from China was responsible for another serious outbreak, during which 12,715 cases were recognized and 9,246 deaths occurred. This epidemic first affected Tonking, causing outbreaks in Hanoi, Haiphong and almost 2,000 small villages. Thence it spread to Annam, and in both these territories was characterized by the wideness of its spread rather than the intensity of its incidence in any one area. In this epidemic Cochin-China and Cambodia escaped, though in 1926 the latter territory had been heavily infected. From Cambodia, cholera has spread up the valley of the Mekong from time to time, and medical writers have pointed out that contamination of rural water supplies has probably played an important part in the spread of the disease. In Indo-China human excreta are largely used as a fertilizer, and the danger of contamination of vegetables by this means is evident. This custom is important in that it indicates that the natives do not understand the danger of acquiring disease through contact with faeces which is axiomatic in the civilized races. The handling of faeces in this way is undoubtedly of great importance in the spread of cholera, typhoid and dysentery, as it has been proved to be in China.

Cholera is largely spread through contamination of water supplies and it is noted that in 1926 only the parts of Saigon which are not served with the main piped water supply were affected. In Cambodia in 1912 there was a drought which caused famine. This not only created a refugee movement, but reduced the available water supplies; the small wells were heavily used and soon became grossly contaminated, with the result that cholera spread rapidly.

In the face of epidemics sanitary measures are taken as they are possible, but the problem is one of great difficulty. The French authorities have relied largely on enormous campaigns of anti-cholera inoculation, and the majority of writers report favourably on this measure, though some are not so enthusiastic. Adequate control, however, can only be achieved by the slow process of control of water supplies and the education of the inhabitants in sanitation and personal cleanliness.

The typhoid group of fevers.—Of these true typhoid is the most common, and a considerable number of cases are reported each year from all parts; in 1937 there were records of 1,279 cases. In Cochin-China it is seen especially in Saigon and the provinces of Giadinh, Bentré, Soctrang and Mytho, and is usually of a rather benign type. In Tonking the incidence appears to be rising; it is said that cases occur in Europeans through the consumption of oysters, and in natives from the eating of vegetables grown near Hanoi in fields fertilized with manure of human faeces. Typhoid fever in Britain is usually a water-borne or milk-borne disease and tends to occur in epidemics; no doubt

the same mode of spread takes place in Indo-China, though definite reports to that effect have not been seen, but spread through the eating of contaminated vegetables is easy to understand.

Dysentery.—Cases of amoebic dysentery have been reported for many years in large numbers, but the numbers confirmed by laboratory examination are but a fraction of those diagnosed on clinical grounds. In 1937 the figures were :—Cochin-China 34,667, Cambodia 19,866, Annam 25,523, Tonking 9,633, Laos 6,159. These figures are very high and it may be that diagnosis is not always accurate. It is noted that liver abscess, a known sequela of amoebic dysentery, is becoming more rare, possibly because specific treatment of the dysentery with emetine is becoming more common. Amoebic dysentery is common in the Tonking delta, but is much more rare in the mountains.

Bacillary dysentery is reported in considerable numbers in Tonking, but there can be little doubt that many cases are not diagnosed. This disease is usually responsible for a high proportion of infant deaths in the tropics.

These diseases are spread by the contamination of food and water with human faecal material, either directly or through the medium of house flies. The remarks on the spread of typhoid apply equally to the dysenteries.

Other Diseases.

Helminthic diseases.—In Indo-China the distribution of *hookworm* infection is uneven. In Tonking and North and Central Annam the proportion of the population infected varies from 50 to 68 per cent. In these parts the dry season is relatively short, and the long duration of the wet season and the corresponding persistence of moisture in the soil are favourable to the embryos. In Cochin-China the rate is 15 to 25 per cent., in South Annam 20, in Laos 29, in Cambodia (when the ground dries thoroughly in the dry season) 17, and in parts of North Annam, where there are salt marshes (inimical to the embryos) not more than 7 per cent. These figures represent the amount of infection discovered ; they do not represent the amount of disease, since light infection is compatible with good health.

Infection with *Strongyloides* is found in Tonking, and 318 cases were reported during 1937. This infection, though not nearly so important as hookworm, should be borne in mind since it appears to be unusually prevalent. It is generally an infection of dogs and cats, but in Tonking, for some reason as yet not clear, it is apparently rare in these animals.

Of the other worm infections, that with the common round worm *Ascaris lumbricoides* is the most frequent, but is rarely a serious condition. The oriental liver fluke *Clonorchis sinensis* is found in the lower parts of Tonking and Annam. This infection is acquired by the eating of raw or undercooked fresh water fish in which the embryos are encysted.

Filariasis and its sequel, elephantiasis, are found. The mosquito carriers of these infections have not been fully reported for Indo-China, but *Anopheles minimus* and *A. jeyporiensis* are mentioned ; doubtless species of *Culex* and *Mansonia* are mainly responsible.

Schistosomiasis has been reported in a few cases, but with reservations.

Sparganosis, an infection of man due to an embryonic cestode, is not uncommon in Indo-China. This embryo is normally a parasite of

frogs and is acquired by man as a result of the native custom of applying split frogs, or compresses made with frog tissue, to inflamed spots, more particularly the eye. The custom is evidence of the influence of Chinese medicine. The reasoning underlying the procedure is interesting :—inflammation produces a heat, the frog is cold-blooded, therefore frog tissue will remove inflammation. Or, alternatively, inflammation of the eye is due to worms, the frog eats worms, therefore frogs applied to the eye will remove the inflammation. Unfortunately, in actual fact, the sparganum is introduced in the process. The secretions of the Malayan bullfrog *Kaloula pulchra* are reputed to be good for silkworm bites, but in reporting this view the French author JOYEUX asks, sceptically, whether a silkworm has ever been known to bite.

Leprosy is well known in Indo-China. In 1937 some 5,000 cases were known to exist, but it was estimated that the full total was probably about 15,000. This is not a particularly heavy incidence rate in comparison with the figures reported from Burma, India and Central Africa, but it is enough to constitute a problem for the health authorities. There are special institutions for leprosy at Hanoi, Bac Ninh and Thai Binh in Tonking, as well as 4 leprosy villages which are conducted under native administrations of their own. In Annam there are institutions at Than Hoa, Kontum, Djiring and Qui Hoa, in Cochin-China at Choquan and Culao Rong, in Cambodia at Treong. There are facilities for isolation in Laos, and in Kwang-Chow-Wan there is one institution.

Tropical phagedaenic ulcer.—The cause of this condition is not definitely known. It is common in labourers and appears to start from small abrasions or wounds of the legs, and may lead to great destruction of the tissues. During 1937 there were 121,543 cases, chiefly from central Annam.

Yaws is widespread and has been noted particularly in the Indo-Malay races of Cambodia, Laos, western Cochin-China and the Annam coast. In Cambodia the incidence is especially high in Kompong-Thom, Benglovea and Battambang ; in Cochin-China there are endemic centres at Giadinh, Thudaumot and Chaudoc. In the whole of Indo-China 97,442 cases were reported during 1937. It is stated that 70 per cent. of infants are affected and that 45 per cent. of adults show late signs of the disease, and that, as so often in the tropics, the natives regard it as inevitable.

Venereal Diseases.—Of these, syphilis is perhaps the most important, 86,093 cases were reported in 1937, of which more than half were found in Annam.

In Saigon 60 per cent., in Hanoi 35 per cent., and in rural districts near Saigon 20 per cent. of samples of the population have been found to give positive results to blood tests for syphilis, but these figures are probably vitiated by the fact that in yaws the same result is obtained with the test. It is noted, however, in spite of the undoubted prevalence of syphilis, that signs of congenital syphilis in schoolchildren are rare. The reason for this rarity of congenital disease is believed to lie in the fact that most of the syphilitic children fail to survive, since congenital syphilis is not uncommonly seen in the newborn in maternity homes.

There are in Indo-China a number of institutions for the treatment of syphilis, and it is part of the duties of the staffs of travelling and fixed dispensaries, and of hospitals, to give treatment throughout the country. Surveillance of prostitutes is attempted.

Gonorrhoea is probably more widespread than syphilis. In 1937 there were 70,000 known cases, but those undetected probably numbered far more. In Saigon almost all the prostitutes examined were infected. This disease is a major problem.

Soft sore accounted for about 15,000 cases in 1937, and *lymphogranuloma inguinale* for about 2,300, being found, in many instances, along with other venereal diseases.

Tuberculosis.—This disease is far more widely spread in tropical countries than in many temperate lands where it is better recognized. It is not yet sufficiently realized that tuberculosis is not only a particularly fatal disease in natives of tropical countries, but also that the proportion of these peoples suffering from the disease in many cases greatly exceeds that found in Europe and North America. In Indo-China it is a problem which has been fully realized by the French, and the extent of the problem is indicated by the fact that during 1935, 35,014 cases, and during 1937, 48,120 cases, were reported. It is not clear, however, whether these represent new cases or include some which had been diagnosed and recorded in previous years. Even should these not all be new cases, however, there can be little doubt that as the figures stand, they understate the position, since even in Europe, where the proportion of doctors to population is high, there still cannot be said to be a fully efficient service of diagnosis of a disease, one of the characteristics of which is its insidious onset. In a country like Indo-China the proportion of doctors to population is much less and it is not possible that all cases of tuberculosis are recognized.

As in other countries, tuberculosis is more prevalent in towns and cities than in rural districts, and for this reason it is stated to be more common in adults of the wealthy or middle classes than in peasants. Malnutrition is regarded as an important factor in the predisposition to tuberculosis, but the French authorities recognize the fact that a more important influence is exercised by the overcrowding which occurs in the dark, airless dwellings, especially of the towns. In these eastern countries there is little tuberculous milk.

The heaviest incidence appears to be in Tonking and Cochin-China, but it is not certain that this is so, since the high figures reported from these areas may be the result of the greater facilities for diagnosis which exist in Hanoi and Saigon than in many other places. The point is that where the facilities exist the cases are found.

To deal with tuberculosis the French have created special hospitals at Lalung Bounaire, Thudaumot, Phulam, Hanoi, Saigon and Hué, and have reserved pavilions or beds for the disease in many other hospitals. In Cochin-China there is a travelling dispensary with X-ray apparatus, and in many parts there are fixed dispensaries. Preventive vaccination by means of BCG has been widely used.

Smallpox.—As in most primitive communities, smallpox is a major problem. It is constantly present in endemic form, and has, from time to time, flared up as widespread epidemics either from the spread of existing foci or as a result of introduction from abroad. Considerable epidemics were reported from Cochin-China, Tonking, Laos and Cambodia in 1917–1920 and in 1924–1925. The latter epidemic followed that which affected the whole of the Far East, India, China, Japan and Siam, in 1923. In 1937 there were 3,000 cases with 680 known deaths.

To cope with this disease the usual port health regulations in regard to immigrants are in force, and vaccination is performed on a large

scale. In 1904 a vaccine institute for the preparation of lymph was created in Hanoi, and now similar centres exist in Saigon, Hué, Vientiane and Xieng-Khouang. Vaccination is performed by trained natives, and millions of people are dealt with each year—in 1928 over 7½ millions were vaccinated. This campaign is continuous.

Of the diseases which commonly occur in temperate climates *influenza* has been reported, sometimes in epidemics. *Pneumonia* is important; it is common in the tropics, not only during influenza outbreaks, but also as a constant and fatal disease. In 1937 there were 6,936 reported cases and the fatality rate in hospital was 32·6 per cent. *Cerebrospinal meningitis* not uncommonly occurs in epidemic form in labour camps. In 1940, 6,788 cases with 819 deaths were reported from Tonking, where the disease became epidemic. *Diphtheria* is found, especially in Cambodia, where there were 123 cases in 1937. Schick tests in schools of Thanhoa showed positive results in only about 4·4 per cent., and in Dalat and Haut Donnai in 18–20 per cent. of the children, indicating a high level of immunity. The disease was not seen in Laos or Kwang-Chow-Wan in 1937. *Measles, chickenpox* and *mumps* occur, the two latter especially in Annam. *Whooping cough* is relatively common and a few cases of *scarlet fever* have been reported from Cochin-China. There was an outbreak of *infantile paralysis* in 1935, when 248 cases were reported; in 1937 there were only 12.

Trachoma is said to affect 5 million of the inhabitants of Indo-China and to be particularly common among the poor. It is associated with childhood and in Pnom-Penh 43 per cent. of the schoolchildren are affected. In Cambodia there is a kapok industry and it is thought that the dust created may, by producing irritation of the eyes, predispose to trachoma. This, however, is mere supposition. In Annam the disease is very common and although in the majority of cases it is mild and chronic, tending to spontaneous cure, it may lead to trichiasis and entropion and to complications which eventually produce impairment of vision. These complications are seen in Kwang-Chow-Wan, though actual trachoma is stated to be rare. It is probable that, as a cause of blindness, trachoma is less important than gonorrhoea; nevertheless it presents a sufficiently serious problem, and anti-trachoma work forms a specific part of the duties of the rural health services. As the disease is associated with poverty, the argument has been used that the standard of life must be raised before improvement is possible, but trachoma is conveyed from man to man by direct contagion, and it is probable that contagion due to the overcrowding and dirty habits of the people is more important than poverty *per se* in this disease.

Rabies of man and animals is found. In Tonking during 1937 there were 19, in Vientiane 3 and in Saigon 2 human deaths from this cause; 62 animals suffered from the disease. At the Pasteur institutes of Saigon and Hanoi, and the laboratories at Hué, Pnom-Penh and Vientiane, 5,663 treatments were given in that year.

Anthrax has been found in past years and was recorded as an epidemic in 1914. There is no recent information, but it probably occurs in cattle and may be contracted by man by the eating of undercooked flesh of animals dead of the disease, or by contact with the skins.

Tetanus was responsible for 286 cases in 1937, but is probably more common than this figure indicates. It is noted that tetanus of the newborn causes a high proportion of infant deaths; it is contracted

through contamination of the umbilical cord, but the incidence is falling, especially in Cochin-China where trained midwives are working.

Alcoholism and drug addiction.—Alcoholism is stated to be widespread in the towns and among those engaged in certain unusually exhausting occupations; in the rural districts it is virtually non-existent. Of the 1,600 cases reported in 1937 the majority were from Cambodia, Annam and Cochin-China. The annual number of admissions to lunatic asylums, due to alcoholism, is very small. Rice spirit is in current use; it is taken in small quantities and, as a rule, only on ritual occasions or at family celebrations.

Opium addiction is rare in the vast bulk of the rural population. Opium smoking is habitual only among the Chinese, a proportion of the wealthy Annamites, and those town dwellers who frequent the squalid dens. Opium addiction is not regarded as an important public health problem and the admissions to hospital on this account are low. There is, of course, a traffic in opium; and smuggling takes place.

Cancer is not rare. The majority of the 2,815 cases reported in 1937 were found in Cochin-China, Annam and Tonking. It is noted that in the majority of cases the external genitalia are involved, and that only 5 per cent. are growths of the alimentary tract.

Venomous animals.—Several poisonous snakes are found in Indo-China, of which the most important are the cobra *Naja naja*, the king cobra *Najah hannah*, the krait *Bungarus fasciatus*, and *B. candidus*. These members of the cobra family are all dangerous, their venom having a powerful action on the nervous system. Of the viper family the daboia (*Vipera russellii*), *Ancistrodon rhodostoma* and *Trimerisurus gramineus* (the banana snake) are dangerous, having a powerful action on the tissues round the bite and on the blood. Other species are found, but are more rare. Pythons are numerous and may attain enormous size, up to 10 yards; these are never poisonous and are said not to attack man. Poisonous sea snakes are encountered.

Spiders and scorpions are common and their bites or stings may produce severe symptoms. Of the biting insects *Brachinus crepitans* is noted; it is said to discharge formalin gas with a loud noise, and to attack man.

Bibliography.

Annales de Médecine et de Pharmacie Coloniales. Annual Supplements of recent years. Les Maladies Transmissibles observées dans les Colonies Françaises et Territoires sous Mandat.

Bulletin de l'Office Internationale d'Hygiène Publique recent years.

FAR EASTERN ASSOCIATION OF TROPICAL MEDICINE. Transactions of the Eighth Congress, Siam. 1930. Vols. 1 and 2.

KERMORGANT, M. Maladies qui ont regné en Indochine en 1915. *Bulletin de l'Académie de Médecine.* 1917. Vol. 77. p. 738.

LEAGUE OF NATIONS. Report on the Prevalence of Epidemic Disease and Port Health Organization and Procedure in the Far East. F. Norman WHITE. Geneva. 1923.

LEAGUE OF NATIONS. HEALTH ORGANISATION. Report on Public Health Services in Various Countries. 1923–1927. French Colonies, S. ABBATUCCI.

LEAGUE OF NATIONS. HEALTH ORGANISATION. Intergovernmental Conference of Far Eastern Countries on Rural Hygiene. Preparatory Papers: Report of French Indo-China. Geneva. 1937.

LEAGUE OF NATIONS. Epidemiological Reports. Recent years.

Revue Médicale Française d'Extrême-Orient, Archives des Instituts Pasteur d'Indochine and *Bulletins de la Société de Pathologie Exotique.* Numerous papers by French and Indo-Chinese authors of recent years.

Tropical Diseases Bulletin recent years. Abstracts of numerous papers by French authors.

SUMMARY OF RECENT ABSTRACTS.*

IX. LEPROSY.

Epidemiology.

In a course of lectures (now published) on leprosy in relation to public health, COCHRANE (p. 785) has laid stress on several generally accepted views : on the importance of close and prolonged contact in the transmission of leprosy to children, on the value of the derivatives of hydnocarpus oil in treatment, and of intramuscular fouadin for the acute lepra reaction. He insists on the necessity for isolation of the most infective patients and advocates voluntary segregation ; for this purpose village isolation is being attempted in Madras, in areas shown by surveys to be seriously affected.

In the Annual Report of the Madras Provincial Council of B.E.L.R.A., AUSTIN (p. 397) once more emphasizes the overriding importance of house and family contact in the epidemiology of leprosy in children. If the incidence in children is higher than that found in adults, the disease is probably spreading.

LOWE (p. 317) remarks that, in an institution in India at which infants are not separated from leper parents until after the age of 18 months, there have been 25 instances of leprosy developing in such children when they attained ages from 3 to 10 years. He therefore advocates separation as early as possible ; adoption from birth by relatives is a good solution. Marriage of lepers of child-producing age should be prohibited in leper institutions unless the male patient is sterilized.

In Orissa leprosy is widespread, especially in the humid coastal districts. VERGHESE and RATH (p. 546) report an incidence of 1·3 per cent. in 226,122 persons examined. Of these, 31 per cent. were lepromatous. The authors advocate the institution of agricultural colonies for the isolation of lepers.

In a series of reports on leprosy in the West Indies, MUIR (pp. 462–4) brings out several important points. Leprosy surveys are needed, since many undetected lepers exist, who do not receive treatment, and who are not under supervision. Some of these patients are in an early stage of disease, others are infective. Follow-up of contacts of lepers should be more widely practised ; this would lead to detection of new cases. Leprosy should be borne in mind during routine examinations of schoolchildren, and the education of medical officers in the signs of early disease, and of the public regarding the curability of leprosy, and its epidemiology, should be undertaken more vigorously. Treatment of early cases apart from cases which are incurable should be arranged, and more modern methods instituted. Certain leprosy ordinances should be relaxed so as to allow patients to receive treatment as out-patients.

McCOY (p. 609) discusses leprosy in the United States, where, except in the States bordering the Gulf of Mexico, the same tendency is evident for the disease to die out as has been observed in parts of Europe. In Louisiana, Florida and Texas, however, there is a strong tendency for the foci of infection to perpetuate themselves.

---

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1943, v. 40. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

Discussing the incidence of leprosy in Maranhão, Brazil, ROSSAS (p. 150) records an incidence rate of 1·2 per 1,000 in one area, rising to 5·7 in another. He notes that the factors leading to high incidence are lack of segregation of lepers, poverty and poor nutrition.

DANTAS (p. 921) contributes a paper on leprosy in the State of Paraíba, Brazil.

In *Leprosy in India* (p. 701) an editorial comment rejects the view that the consumption of colocasia (taro) plays a part in the causation of leprosy, and states that there is no valid reason why the production of this article of diet should not be encouraged. The theory, originally advanced by OBERDÖRFFER, that the incidence of leprosy is related to the predisposing effect of a diet rich in articles (such as yams in warm climates, or corncockle in Europe) which contain sapotoxin, is accepted by GEHR and GEHR (pp. 59, 60). It is suggested that the sapotoxins act by disturbing the endocrine functions of the body, and it was on the basis of this theory that the treatment of leprosy with diphtheria toxoid was conceived, the supposition being that adrenal insufficiency predisposes to infection by leprosy [see this *Bulletin*, 1941, v. 38, 26]. These authors have studied the distribution of the disease in the Balkan countries and in Spain. There is high incidence in Crete and other Grecian islands, and in these places the consumption of sapotoxin-containing foods is said to be high. The predisposing factors regarded as important by most leprologists are more or less dismissed in favour of this sapotoxin factor. In Spain, leprosy is most prevalent in the southern and Mediterranean provinces, and in Portugal around Coimbra.

DENECKE (p. 149) has studied leprosy in the Spanish West African colony of Rio Muni, where it is widespread in the moist, hot, forested area, and in the island of Fernando Po. His investigations do not support any idea of hereditary transmission, and he inclines to the view that the common method of infection is through wounds. He does not subscribe to the sapotoxin theory, but thinks that a generally poor diet, deficient in animal protein, is a predisposing factor. Leprosy in the wives of lepers seems to affect adversely the birth rate, but child mortality is as high in the children of healthy as of leprous wives of lepers.

MUÑOZ RIVAS (p. 151) has examined the stomach contents of fleas which had fed on lepers, and has found acid-fast bacilli in a large proportion of them. This investigation was part of an enquiry into possible insect transmission of the disease, in which fleas were selected because of their ubiquity and habits. Other arthropods are also discussed, but are not considered important; the author makes no claim that fleas do, in fact, transmit leprosy; he merely records his preliminary findings. [LAMBORN (this *Bulletin*, 1935, v. 32, 909; 1937, v. 34, 610) has also investigated this arthropod transmission of leprosy.]

Aetiology. Pathology. Lepromin Tests.

DUBOIS and GAVRILOV (p. 150) have failed in an attempt to infect 16 hamsters with material from human leprosy. One animal developed lesions containing acid-fast bacilli, but these proved to be rat leprosy bacilli. The authors cannot yet offer an explanation of this, but are investigating the matter further.

COCHRANE (p. 151) describes the cellular reactions in the various forms of leprosy; these are strong in the neural forms, and are illustrated

by the tuberculoid and tissue reactions which lead to destruction of the bacilli. The absence of such reactions in lepromatous leprosy enables the organisms to multiply and spread. In nerve leprosy the tuberculoid cellular reaction may lead to the formation of abscesses within the nerve sheaths. These abscesses may damage the nerve fibres and lead to permanent destructive changes.

CASTAÑE DECOUD (p. 547) describes a condition of para-arterial neural infiltration in tuberculoid leprosy, in which infiltration starts around the nerve fibres and displaces, but does not invade, the vascular structures. This condition is not found in non-leprous granulomata.

MARTÍNEZ BÁEZ (p. 922) describes the Lucio form of leprosy, a form originally investigated by Rafael Lucio in Mexico, and since given little attention. In the dermis are masses of "inflammatory cells" around the blood vessels, the vessels are dilated and changes are present in their walls and in the endothelial cells of the capillaries. The endothelial cells contain leprosy bacilli. The cell aggregations consist of lymphoid elements and histiocytes, and may undergo necrosis. The sweat glands may be involved.

SCHUJMAN and VACCARO (p. 547) discuss glandular enlargement in leprosy. The order of frequency of enlargement in their series was axillary, inguinal, cervical and epitrochlear; the glands did not suppurate. They were largest and most numerous at the time of a leprous reaction. Enlargement was present in 96 per cent. of lepromatous, and in 60 per cent. of tuberculoid, cases. There seems to be no relation between the severity of the skin lesions and enlargement of the glands draining the area.

GONZALEZ GUZMAN (p. 787) has studied the lymphocytes in the blood of lepers. The picture does not appear to be very characteristic—most of his patients had a total of lymphocytes within the normal limits—but he states that there is a nucleolar deviation to the right [this connotes an increase in the number of lymphocytes having several nucleoli.]

FITE (p. 787) makes the point that tuberculoid leprosy represents the natural development of immunity to its highest point. The reactions of leprosy are allergic manifestations, in which hyperergic inflammation makes apparent old lesions in the guise of new ones.

FERNANDEZ and OLMOS CASTRO (p. 245) have studied the reactions of lepers and other persons to the intradermal injection of whole lepromin (a preparation which contains all the constituents of a leproma) and of lepromin filtrate (a preparation made from a leproma and then passed through a filter candle). Whole lepromin gives rise to an early reaction and a late reaction (Mitsuda). If the early reaction is positive, the late reaction is also invariably positive, but in some cases the late reaction may appear without having been preceded by an early reaction. The early reaction is never seen in lepromatous cases; both reactions are frequently positive in neural leprosy, and more frequently still in tuberculoid leprosy. In healthy persons the results are often divergent, the early reaction usually negative, and the late reaction often positive. The lepromin filtrate produces the early, but not the late, reaction, and the results are very similar to those of the early reaction with whole lepromin. This filtrate acts in much the same way as DHARMENDRA's soluble proteins of *Myco. leprae.*

DHARMENDRA (p. 548) has prepared from lepromatous tissue a bacillary antigen from which tissue elements and lipoids have been very largely eliminated. The antigen consists almost entirely of bacilli,

and is found to retain its antigenic property. It can be standardized. With this antigen the early reactions are stronger, and the late reactions considerably weaker than with ordinary lepromin; most neural cases respond to this antigen, and most lepromatous cases do not.

DHARMENDRA *et al.* (p. 316) note a tendency for the lepromin reaction to vary somewhat according to whether the test is applied for the first or second time, and according to the seasons of the year. Standardized lepromin shows little variation in activity. They (p. 317) cannot confirm the view that a negative test is converted to positive by repeated injections of lepromin.

DHARMENDRA and MUKHERJI (p. 701) have found that the activity of tuberculoid neuro-macular leprosy undergoes exacerbation particularly in the four months of the hot, dry season, February to May. During the phase of activity the lepromin test shows strong reactions. Climatic conditions do not, apparently, explain the exacerbations, nor does the consumption of colocasia; the causation of these seasonal variations is therefore not clear.

Clinical Findings. Treatment. Prognosis.

FAGET (p. 847) discusses the high incidence of pulmonary tuberculosis in lepers in the leprosarium in Louisiana, and at Culion. The finding of acid-fast bacilli in sputum does not suffice for diagnosis, since they may be leprosy bacilli from throat lesions. Animal inoculation must therefore be practised. X-ray examination of the chest is important for diagnosis of tuberculosis and it is noted that leprosy lesions of the lung tissue are rare, and are too small to be detected by X-ray. Treatment for tuberculosis should be given in the usual way, and active anti-leprosy treatment should be stopped. Prognosis as regards tuberculosis is fairly good. It is most important that the tuberculous patients should be isolated to prevent infection of others.

FIDANZA (p. 788) has recorded two cases. In the first a rash, considered to be syphilitic, turned out to be due to leprosy; in the second the reverse was the case.

DEGOTTE (p. 397) describes an ingenious modification of the sweating test in nerve leprosy, in which a permanent record of an anhydrotic area is made by applying transparent paper, coated with 5 per cent. silver nitrate in gelatin, to the area after injection of pilocarpine. Chlorides in the sweat react with silver nitrate to form silver chloride, which turns black in the light. After treatment in a bath of paraffin these records can be kept, for comparison with later records.

AUSTIN (pp. 315, 700) contributes reports on the Central Leper Hospital, Makogai, in which he noted that intramuscular injections of iodized chaulmoogra oil and intradermal injections of ethyl esters remain the routine treatment. He remarks that a large proportion of very early cases are sent to Makogai from the Cook Islands by a practitioner who was trained at Makogai; a corollary is that it is among these patients that the highest proportion of arrested cases is achieved.

MONTEL (p. 789) reports apparent cure in three patients with neural leprosy and observed for several years after cessation of treatment. At the time of diagnosis the disease was progressive, and the favourable course is attributed by the author to the use of a preparation of chaulmoogra.

Successful results in the treatment of a few cases with Caloncoba oil are reported by RADNA and LIMBOS (p. 316), but further experience

is necessary before a true appreciation can be made. Caloncoba oil is rich in substances of the chaulmoogric acid series.

A trial of sulphanilamide in leprosy has left FAGET *et al.* (p. 610) with the impression that, although it is useful in secondary infections, it has no value for the leprosy itself.

Investigating the effect of sulphanilamide and sulphathiazole on rats and mice infected with a virulent mouse strain of lepra bacilli KRAKOWER *et al.* (p. 789) found that administration over a period of one year prevented the development of any but very small lepromata, whereas in controls there were large lepromatous masses, with ulceration and metastases. If treatment was continued for 5–7 months only, the animals developed more extensive lesions, but still not so great as those of the controls ; the same was true of animals in which treatment was not commenced for 5 months after infection. Bacilli from the treated animals were shown to be of unimpaired virulence, and were not sulphonamide-fast. There was no evidence that the bacilli were killed by the treatment, only that there was retardation of their effects.

IGNACIO CHALA (p. 248) has used an antimonial, Stibicol, with some appearance of success, in the treatment of three patients with tuberculoid or macular leprosy.

REENSTIERNA (p. 152), by injecting into sheep a strain of acid-fast bacillus, isolated from a case of human leprosy, and regarded by him as the cause of leprosy (though possessing the characters of the rat leprosy bacillus) has produced a serum which has been tried in the treatment of leprosy, in many countries and by many workers. He has published an account of the results achieved, and his conclusions may be summed up in the statement that in nerve leprosy rapid amelioration of sensory and paralytic symptoms, healing of ulcers (alone) and occasional improvement of macules often follow the treatment. There is, as yet, not enough evidence to indicate the duration of these results, but the author claims that the serum may be of some value as an adjuvant to other forms of therapy.

GRASSET and DAVISON (p. 611) have prepared an antigen from a non-acid-fast bovine strain of *Myco. tuberculosis*, which they have used in the treatment of tuberculosis and which they have now tried in leprosy. It is not useful in lepromatous cases, but seems to have a value in nerve leprosy if used in conjunction with hydnocarpus esters. The majority of the patients with nerve lesions became bacteriologically negative, whereas in a comparable number of controls this did not occur.

TRANT (p. 154) has tried diphtheria antitoxin in early leprosy and considers that the effects on local lesions were moderately encouraging. In maculo-anaesthetic cases the results were more disappointing.

HAYTHORNTHWAITE (p. 702) has found that injections of lactoflavine four or five times in the course of a year have prevented the formation of bullae (which lead to painful ulcers) in a number of cases, and that it is very effective in the treatment of bullae when formed. The condition is not associated with other signs of vitamin B_2 deficiency. A light plaster support affords great relief in cases of perforating ulcer of the foot without bone disease.

PERVES (p. 155) has infiltrated with 2 per cent. novocaine the inferior cervical, or stellate, ganglion of the sympathetic in the treatment of nerve lesions of the arm. The results include recovery of the functions of the fingers, absorption of oedema and healing of ulcers.

The method is based upon the proved value of such treatment in trophic and sympathetic lesions in general.

In a discussion of the prognosis of leprosy, COCHRANE (p. 151) points out that there is a strong tendency for the mildest nerve forms to recover spontaneously. Improvement without treatment occurred in 53·1 per cent. of patients with macular, tuberculoid, or incipient childhood lesions; it was 3–5 times as frequent in patients with positive lepromin reaction as in negative cases. Neural leprosy rarely became lepromatous.

MANALANG (p. 465) gives an account of the condition of lepers released from Culion and the provincial centres in the Philippines between 1922 and 1938. This cannot further be abstracted, but, considering the advanced condition of so many of the Culion cases, the results here recorded are encouraging.

Classification.

PARDO-CASTELLO and TIANT (p. 785) have devised a classification of leprosy in which not only the clinical manifestations, but also the pathology, immunology and bacteriology, are taken into account. No adequate description of this classification can be given in a short space, and readers are advised to seek the details in the original abstract. *Charles Wilcocks.*

RABIES.

A REVIEW OF RECENT ARTICLES. XLI.*

i. *Virus.*

REMLINGER and BAILLY[1] discuss further their theory that proteolysis is responsible for the inactivation of the fixed virus of rabies under certain conditions of desiccation. In previous papers [this *Bulletin*, 1940, v. 37, 615; 1943, v. 40, 195] they stressed the fact that the virus, contrary to previous belief will remain infective for long periods after rapid desiccation *in vacuo*. On the other hand during the process of slow desiccation over caustic potash, as carried out in the preparation of Pasteur's vaccine, there is complete loss of infectivity of the virus in a few days. They maintained that this loss of infectivity was probably due to the action of cellular proteolytic ferments or enzymes, similar to those responsible for the maturation of meat and the destruction of carcasses. In support of this hypothesis they submit, in the present paper, the result of an experiment in which a 1 : 200 suspension of the brain substance of mice, dead after infection with fixed rabies virus, was filtered through filter paper and then mixed with varying concentrations of ascorbic acid. The mixtures of virus and ascorbic acid and control suspensions of virus without ascorbic acid, the hydrogen ion concentration of both having been adjusted to 6·8, were kept in the dark at a temperature of 21°C. to 24°C. in the "absence of

---

* For the fortieth of this series see this *Bulletin*, v. 41, p. 167.

[1] REMLINGER, P. & BAILLY, J. Action de la protéolyse sur la virulence de la substance nerveuse rabique. *Ann. Inst. Pasteur*, 1943, May–June, v. 69, Nos. 5–6, 135–8.

oxygen" (such reduction as was effected resulted from allowing a candle to burn in an hermetically sealed incubator in which the tubes were placed). Care was taken to exclude any copper ions from the fluids in which the suspensions were made. It is stated that under similar conditions it has been shown by other investigators that ascorbic acid will inhibit certain proteolytic ferments such as polypeptidases. The results obtained by the present authors pointed to a longer survival of the virus in the mixtures containing ascorbic acid up to 1 : 1,000 than in the mixtures containing ascorbic acid in 1 : 5,000 or greater dilutions, or in the suspensions without ascorbic acid. They conclude that this could be explained by the probable inhibitory action on the proteolytic ferments. They are aware that AMATO [this *Bulletin*, 1938, v. 35, 653] reported that in controlled experiments ascorbic acid destroys the fixed virus of rabies *in vitro*. However, they maintain that he did not ensure those conditions referred to above which would serve to obviate the production of hydrogen peroxide as a result of the oxidation of ascorbic acid, and that FERMI has shown that hydrogen peroxide will inactivate the fixed virus of rabies.

[While their hypothesis and their conclusions that Pasteur, in making his vaccine, "employed the ideal conditions to secure diastatic attenuation of the virus before desiccation destroyed the ferments," may be correct, it would appear that the problem requires further investigation and the results may be open to other and simpler interpretations. It may here be recalled that REMLINGER & BAILLY (this *Bulletin*, 1940, v. 37, 615) recorded that whereas the viruses of rabies and Aujeszky's disease would both survive for long periods after being dried rapidly, they behaved dissimilarly to the action of slow desiccation over KOH. The virus of Aujeszky's disease was "50 times more resistant" to the latter than the fixed virus of rabies. The explanation of these observations solely in terms of the action of proteolytic ferments would not appear to be fully justified.]

KUBES and GALLIA[2] describe a brain-tissue neutralization test, to demonstrate the neutralizing power *in vitro* on rabies virus of the brain tissue of mice treated with anti-rabies vaccines, and compare the results with those obtained in protection and serum-neutralization tests. Their main general conclusion is that "the results given by the brain-tissue neutralization test *in vitro* are closely paralleled by those of the protection test *in vivo* and seem to be equally exact and sensitive." Further, "because of its greater specificity (presumably as compared with the serum neutralization test) and very simple technique, it appears to be a laboratory method of practical usefulness for the evaluation of the antigenic power of anti-rabies vaccines as well as for the immunological differentiation of heterologous rabies viruses." It, would appear, nevertheless, from their results, that it has no advantage either in simplicity of technique or economy of mice used, over the protection test.

Their methods and materials were as follows:—Swiss white mice, 4 weeks old, were immunized according to WEBSTER's method [this *Bulletin*, 1940, v. 37, p. 194]: *i.e.* 6 intraperitoneal injections of 0·25 cc. of the vaccine under test were given, and in one case 6 doses of 0·02 cc. of the vaccine were injected intracerebrally. Eight different

[2] KUBES, V. & GALLIA, F. Brain-Tissue Neutralization. A New Biological Reaction for Rabies Virus. Its relation to the Protection and Serum-Neutralization Tests. *Canadian J. Comp. Med.* Gardenvale, Quebec. 1944, Feb., v. 8, No. 2, 48–60. [10 refs.]

vaccines were used and these consisted of 50 per cent. suspensions of bovine brain tissue in 1 per cent. carbolic acid, diluted 1 : 9 before use. Attenuation of vaccines was effected by storage in the cold for some weeks or incubation at 37°C., and inactivation by incubation at 37°C., 56°C., or, as in one instance where there was no carbolic acid in the vaccine, the virus was neutralized by the addition of an immune serum. Seven of the vaccines were prepared from a native fixed strain of bovine paralytic rabies, " Bolivar " strain, and one from a Pasteur fixed virus strain. The brain-tissue from which the vaccine was made was thoroughly homogenized by passing it first through a Latapie mincer and then through a colloidal mill. With each vaccine, 25 mice were immunized and, 14 days after the first injection, the protection test according to the method of HABEL [this *Bulletin*, 1941, v. 38, 161] was carried out on 20 mice. The remaining 5 mice were bled to death according to KUHN's method [from the axillary artery] (see KUHN, *Science*, 1941, v. 93, 504). Their sera were used in the serum neutralization test and their brains in the brain-tissue neutralization tests *in vitro*. The cross-immunity tests between the Bolivar and the Pasteur strain were carried out on groups of 50 mice. For serum neutralization tests the serum was used undiluted or diluted 10^{-2} and 10^{-3}. The virus-containing mouse-brain tissue was used diluted 10^{-2} or 10^{-3}, the diluent always being saline. The different serum dilutions were mixed with the two dilutions of virus in equal proportions, 0·5 cc. of each, and the mixtures remained at " room temperature " for 18 hours ; 0·03 cc. of each mixture was then injected intracerebrally into mice. Control mixtures consisted of serum of normal mice with similar dilutions of virus in equal proportions.

The brain-tissue neutralization test was similar in general lines to the serum neutralization test. Mouse brain tissue from immunized mice was suspended in saline to give a dilution of 1 : 3 and mixed with 0·5 cc. of serial dilutions of virus. To each tube 2 drops of fresh rabbit serum were added. As a control, a suspension of normal mouse brain tissue was used.

Five experiments were made and, since many conclusions are drawn by the authors from these few experiments, it may be useful to summarize their results in the form of a simplified table (below) which, in the reviewer's opinion (and, it is hoped, in that of the authors also) represents with some degree of accuracy their observations.

They have reported on the results of their experiments as follows :—

Experiment 1.—Both vaccines containing active virus had a high degree of immunizing power. The serum antibodies were of high titre in both groups of mice. The brain-tissue neutralization test showed likewise a high titre of antibodies in the brain tissue of both groups of mice but lower than in the serum.

Experiment 2.—Vaccines (non-infective by I.C. test) with a high protection power elicited also the formation of rabies antibodies in the brain. " However, their antibody-formation power was a little lower than the similar power shown by antirabies vaccines with an active-virus content. The serum neutralization test did not show any reduction of the seric antibody formation power of these vaccines, compared with the intensity of antibody formation seen in Exp. 1."

Experiment 3.—Considering the results of experiments 1 and 2 in conjunction with experiment 3, it is clear that " the number of minimal lethal doses (m.l.d.) withstood by immunized mice *in vivo* is always

Table summarizing KUBES *and* GALLIA'S *Experiments.*

Exp. 1. (6 I.P. injections 0·25 cc.)	*Exp.* 2. (6 I.P. injections 0·25 cc.)	*Exp.* 3. (6 I.P. injections 0·25 cc.)	*Exp.* 4. (6 I.P. injections 0·25 cc.)	*Exp.* 5. (6 I.C. injections 0·02 cc.)
Vacc. 1. (Active virus killed 100 per cent. mice I.C.)	Vacc. 3. (Non-infective - I.C. test in mice)	Vacc. 6. (Non-infective - I.C. test in mice)	Cross immunity tests	Vacc. 3. and Vacc. 4 (see Exp. 2.)
Stored 5 weeks in cold room	Incubated 3 days at 37°C.	Stored in cold 18 months	Pasteur Strain X Bolivar Strain	
P. +++++ B.N. ++ S.N. ++++	P. +++++ B.N. + S.N. ++++	P. 0 B.N. 0 S.N. ++	P. immunological difference indicated	P. ++ B.N. ± S.N. 0
Vacc. 2. (Active virus killed 50 per cent. mice I.C.) Incubated 24 hours at 37°C.	Vacc. 4. (Non-infective - I.C. test in mice) Incubated 7 days at 37°C.	Vacc. 7. (Non-infective - I.C. test in mice) Virus neutralized by immune serum	B.N. immunological difference indicated	
P. +++++ B.N. ++± S.N. ++++	P. +++++ B.N. +± S.N. ++++	P. 0 B.N. 0 S.N. 0	S.N. no indication of immunological difference	
	Vacc. 5. (Non-infective - I.C. test in mice) Incubated 1 hour at 56°C.			
	P. +++++ B.N. +± S.N. ++++			

I.P.=intraperitoneal injection. I.C.=intracerebral injection. P.=protection test. B.N.=brain-neutralization test. S.N.=serum neutralization test

much higher than the number of m.l.d. neutralized by the respective suspensions of brain tissue *in vitro*. Nevertheless there is an actual parallelism between immunity and brain-tissue neutralization. The results of the serum neutralization tests are different; they were positive even when the other two tests gave negative results."

"This fact gives some basis to the supposition of a different character or origin of rabic antibodies present in the serum and those found in brain tissue."

Experiment 4.—The results of this experiment showed that the brain neutralization test gave the same result as the protection test. On the other hand the serum neutralization test did not show an immunological differentiation. "From this fact one may assume that it is due to the different origin of the tissue and seric antibodies and to the greater specificity of the first ones."

Experiment 5.—"Repeated intracerebral injections of killed antirabies vaccine gave a certain degree of immunity to mice. The neutralizing power of the brain tissue of these animals *in proportion* [italics are the reviewer's] with that of the serum, was greater than when the same vaccine was intraperitoneally injected" [Exp. 2.]. "We suppose that it is due to the influence of the direct stimulation of brain-tissue, leading to the local production of cerebral antibodies neatly independent of the antibodies of humoral origin."

These observations have been quoted in some detail since the authors are obviously raising again the vexed question of a tissue as distinct from a humoral immunity, for they state that "there is no doubt left that these results agree completely with the criteria of Centanni, Lépine, *et al.* These authors believe that the virus destructive power of immune serum is not the main support of antirabies immunity *in vivo*." [What LÉPINE says (and the view has been advanced and upheld by others) in his article on rabies in "Les ultravirus des maladies humaines" (LEVADITI, C. and LÉPINE, P., Librairie Maloine, Paris, p. 458) is :—"There is no parallel between the serum antibodies which arise in the reticulo-endothelial system and the state of immunity inherent in the tissue defence of the cerebro-spinal axis. In rabies as in the case of other neurotropic viruses the immunity is of a cellular order and not of a humoral order. It is possible that the rabicidal antibodies play a rôle of completion in the defence of the organism, nevertheless, they are only an epiphenomenon in the establishment of immunity which does not require their presence to manifest itself and which persists long after their disappearance."]

The present authors state also that "the different sensitiveness between the serum neutralization test and the brain-tissue neutralization test, possibly is the best evidence at hand that in the organism, besides the humoral antibodies, there are other antibodies in the brain-tissue which have a greater specificity. If the brain antibodies were a mere local reflex of the serum antibodies it is not likely that the brain-tissue neutralization test could be of a greater specificity and reveal an immunological difference between two heterologous viruses which the serum neutralization test did not show."

They express the opinion also that the possibility of demonstrating a tissue immunity independent of a humoral one may be governed by the greater affinity of a virus for a given tissue [*cf.* results of other investigators in equine encephalomyelitis virus (American) in which the specific affinity is not so great]. Further "a fact remains to be explained. Constantly, the number of m.l.d. neutralized by brain tissue was

lower than the amount of m.l.d.'s neutralized by the serum"—possibly cerebral antibodies "exist within the cells and their neutralizing power is closely dependent on the cellular metabolism. Therefore, their action *in vitro* can be only a fraction of their possible full neutralization power in a living organism. The higher specificity of tissue antibodies may be also explained by the just mentioned nature of the cerebral antibodies. Such an explanation must not overlook the possibility of this greater specificity as being the result of a special and more specific antigen, differing from the antigen arousing the formation of humoral antibodies."

[There is no space here to comment fully on their results and general conclusions. It is felt, however, that the experiments are unfortunately too limited for reliable deductions to be drawn but it is possible that further observations may help to substantiate their contentions.

Attention should be drawn to the following facts :—in Experiment 5, although they have not stressed the point, the amount of antigen injected intracerebrally was about one-tenth of that injected intraperitoneally in Experiment 2. It may be due to this that the immunity response was very much less in the first case than in the second. In Experiment 5 the difference between the brain-tissue neutralization test and the serum neutralization test is not very great, both indicate a lower grade immunity, as does the protection test, than that observed in Experiment 2. There would appear to be no clear evidence that the neutralizing substances detected in the brain tissue were produced locally as suggested. In the field of immunology there is some evidence that antibodies may be formed not only in the reticulo-endothelial system generally, but also in lymph glands. It must be remembered also that when an inoculum is given intracerebrally there is damage to the haemato-encephalic barrier, and antibodies produced elsewhere may be mobilized at the site where some reaction is taking place. In Experiment 4 the results of the cross-immunity tests do not confirm the observations made in the previous paper by the authors (this *Bulletin*, 1943, v. 40, 208) that a vaccine prepared from the fixed native virus of paralytic rabies (Bolivar strain) protects against the Pasteur strain of fixed virus, whereas a vaccine made from Pasteur fixed virus does not protect against a Bolivar virus. In the present experiment the vaccine prepared from either strain did not appear to show much protection against the other. It is noteworthy also that in Experiment 4, the serum neutralization test did not differentiate immunologically between the two strains of virus, whereas in their previous paper (*loc. cit.*) it did so. The only difference was that the serum on the previous occasion was obtained from mice which had survived the protection test and had therefore received an intracerebral inoculation of active virus after immunization, whereas in the present instance the serum was collected from mice which had received a course of vaccine only.

The immunological difference which appears to exist between the Bolivar strain of virus recovered from cases of paralytic rabies in bovines and the Pasteur or other strains of rabies virus recovered from canines awaits confirmation. If, as the authors have tentatively suggested, the degree of fixation or number of passages in the experimental animal may influence the result of such differentiation, this is a factor which would have to be taken into account. In their previous paper (*loc. cit.*) they have stated that "the discrepancies between the present findings and those of preceding workers which did not disclose any biological difference between the canine rabies virus and the paralytic rabies

virus [see *e.g.*, HURST and PAWAN (this *Bulletin*, 1932, v. 29, 595) and MIGONE and PEÑA, *Bull. Soc. Path. Exot.*, 1932, v. 25, p. 590; also GALLO and ITURBE, *Rev. Med. Vet. Parasit.*, Caracas, 1939, v. 1, 91, referring to paralytic rabies in Venezuela] are explained in the writers' opinion by the dissimilarity of the methods made use of."

It is not the reviewer's intention to suggest more than that the present authors' statements should be treated with an open mind. They have recorded observations suggesting that there may be immunological differences (quite apart from immunogenic differences) between strains of the virus of rabies and suggesting the existence of a tissue as distinct from a humoral immunity, a conception which may go counter to current immunological thought. Such stimuli are not to be deprecated simply because they may cause a "flutter in the dovecote" of the "humoralists." However, it would appear that a great deal more experimental evidence is necessary to establish the validity of their conclusions. That there is a lack of parallelism, especially in certain diseases such as poliomyelitis, rabies, Borna disease and foot-and-mouth disease, etc., between the existence of demonstrable circulating antibodies and the degree of resistance to infection by contact exposure or inoculation, does not appear to be in doubt. That such resistance can be exhibited long after antibodies can no longer be demonstrated in the circulation is apparent, but this lack of correspondence is subject to different interpretations, and up to the present no explanation which has been submitted appears to be entirely satisfying.]

ii. *Symptoms and Diagnosis.*

MOHSIN ALI ABBASI[3] reports that a young man of 35 was bitten on the right ear by a "wild mongoose." The victim showed symptoms 57 days later. He reported that there had been some pain around the scar at the site of the wound for a period of two days previously. The patient was restless and had a look of anxiety, and on being presented with water, exhibited typical symptoms of hydrophobia. The following day the condition was worse, the patient was drenched with perspiration and there was considerable salivation. Death ensued a few hours later, the patient being unable to swallow during the final stages. No post-mortem diagnosis was made but there appears to be no reason to doubt that the disease was rabies in view of the history, symptoms and information that the same mongoose bit a cow on the nose on the same day as it attacked the man and the cow died of rabies 12 days before the man. The author believes that this is the first case of a mongoose bite causing rabies. [While this may or may not be true for India, it has, of course, been known in S. Africa since 1929 that the genet or meerkat (*Genetta felina*) and the mongoose (*Cynictis penicillata*) (also known as the yellow mongoose, yellow meerkat or red meerkat) may carry the virus of rabies and infect man, and sometimes cattle by their bites (DU TOIT, *Pan. African Agric. and Vet. Conference Pretoria*, 1929, 272–284).]

PHILLIPS[4] records the history of a case of hydrophobia which followed an attack by a rabid jackal during which five deep bites were inflicted on the head of the victim. The patient had undergone a full intensive

---

[3] MOHSIN ALI ABBASI, M. Mongoose Bite and Hydrophobia. *Indian Med. Gaz.* 1943, Nov., v. 78, No. 11, 550.

[4] PHILLIPS, J. W. Hydrophobia after Anti-Rabic Treatment. *J. Indian Med. Ass.* 1943, Oct., v. 13, No. 1, 26.

course of vaccine treatment for 14 days and the first symptoms were observed 6 days after completion of this treatment. There was a history of premonitory symptoms, during a period of 36 hours before the patient reported sick, of insomnia, headache and vomiting of a coffee-coloured vomit. Incomplete paralysis of the lower limbs set in, spasms of the muscles of deglutition and at times a sort of maniacal fury. Death ensued in two hours. The author is of the opinion that in cases of head bites, even although they may involve the face and neck, in view of the close proximity to the brain and large nerve trunks, cauterization should be carried out in addition to vaccine therapy.

iii. *Methods of Treatment and Statistics.*

KAISER[5] believes that it should be possible to improve the method of preparation of anti-rabies vaccine. His remarks are somewhat diffuse, as is his description of the method which he suggests. His main contention is that the essential part of the process is to get rid of the lipoid portion, the "Ballaststoffe" or "non-specific carrier substance," of the nervous tissue by extraction with ether, thus making the material "hydrophile" or, more correctly, lyophilic. As far as can be gathered the brain and cord material are first dried at low temperature after thorough grinding of the minced tissue in a ball mill for 12 hours and subsequent centrifugation for 30 minutes at 3,800 revs. per minute (see KAISER, *Arch. Virusforsch*, 1939, v. 1, 85). The material is treated with ether in a shaker and then the ether is removed. Sometimes the deposit which constitutes the vaccine is still infective and it has to be treated with iodine vapour by the method previously described by the author (*Arch. Virusforsch*, 1939, v. 1, 237). That the vaccine is non-infective is controlled by the intracerebral inoculation of rabbits. The vaccine is in the dried state and is therefore compact and the risk of bacterial contamination is avoided. It can be distributed in phials containing one dose which can be easily dissolved in the prescribed quantity of physiological saline. This method of preparation of the vaccine facilitates decentralization of the rabies service. The vaccine contains no carbolic acid and it is free also of admixture with anything superfluous. [There are many different methods of preparing rabies vaccines, and until recently there was no reliable test available to gauge the potency of these. Now, however, there is a considerable amount of evidence that a mouse potency test, such as that elaborated from other methods by HABEL [this *Bulletin*, 1941, v. 38, 161] gives a good indication of the probable efficacy of a rabies vaccine in protecting other animals, *e.g.*, dogs, and it would be useful if tests of this sort were carried out on all vaccines for human application. It would be especially so when some new method of vaccine production is introduced, as in the present instance, which deviates somewhat from methods in more common use.]

BÉQUIGNON and VIALA[6] report that during the year 1942, 435 people presented themselves for treatment with vaccine at the Pasteur Institute, Paris, and that in 149 of these such treatment was considered necessary. Forty-seven had been bitten by dogs (in 8 instances the

---

[5] KAISER, M. Ist es möglich, die technische Herstellung von Lyssaimpfstoffen zu vervollkommnen? *Wien. klin. Woch.* 1943, Aug. 27, v. 56, No. 33/34, 507/8.

[6] BÉQUIGNON, R. & VIALA, C. Les vaccinations antirabiques à l'Institut Pasteur en 1942. *Ann. Inst. Pasteur.* 1943, Nov.–Dec., v. 69, No. 11–12, 372–4.

dogs were strays), 26 by cats (in 9 instances by stray cats) and 6 by rats; 148 patients belonged to Category C (*i.e.* the animal responsible for the bite was suspected of being infected with rabies), and one belonged to Category B (*i.e.* rabies had been diagnosed by the clinical picture in the biting animal). In 145 cases the bites were deep, in 70 they were not through clothing. Eleven bites were about the head, 74 were on the upper limbs, 2 on the trunk and 62 on the lower limbs. There were no paralytic accidents as a result of the vaccine treatment and no deaths were recorded. In 100 cases treatment commenced within 4 days of the bites, in 17 within 5–7 days, in 21 within 8–14 days, in 7 within 15–21 days; in 4, more than 21 days had elapsed. A histological examination of the nervous system of the biting animal was carried out in 38 cases and this included a study of the plexiform ganglion. Since symptoms had not been observed and the histological findings were negative, treatment was interrupted in five cases.

In the fortieth review of this series [this *Bulletin*, 1944, v. 41, pp. 167–181] the results recorded by SHAUGHNESSY and ZICHIS in a paper on "Prevention of Experimental Rabies" were discussed. The reviewer has received a letter and a corrected reprint from one of the authors pointing out that several errors had crept into the paper in addition to the one to which attention had been drawn in the review. However, fortunately, these were minor ones and did not materially affect their general conclusions with the exception of the latter. It is only fair, therefore, to quote their statement that "sixty guinea-pigs were employed as the untreated controls in the experiments in which the animals were treated 6 hours after they were inoculated with rabies. According to these figures 35 per cent. of the control animals did not develop rabies, as compared with the 63 per cent. of those treated with Fuming Nitric Acid and 66·6 per cent. of those treated with Soap Solution." [In the original paper the number of controls which were recorded to have survived was 41/60 and the reviewer made a total 31/60 whereas it should have been 21/60.] It is apparent, therefore, that treatment with Soap Solution or Nitric Acid had some definite but lesser effect even when carried out 6 hours after infection, and the comment appearing in the review requires amendment.

iv. *Post Vaccinal Paralysis.*

STEINBERG and CRIVELLARI[7], at a conference on endemo-epidemic diseases at Buenos Aires, summarized the types of paralytic accidents accompanying or following upon vaccine treatment in rabies and made reference to the known theories as to their aetiology. They referred to the three better-known types, dorso-lumbar myelitis, Landry's ascending paralysis, and peripheral neuritis of the cranial nerves, and to a fourth type, described by Ford as disseminated encephalomyelitis. They gave the detailed history of two cases which they had observed and classified in the category of dorso-lumbar myelitis, although the first of these they thought could be more correctly described as one of encephalo-meningo-myelitis. The patient had been bitten by a dog, but it was not certain that it was rabid. Thirteen days after the course of vaccine treatment commenced there was general hyperreflexia, emprosthotonus ("couché en chien de fusil"), some nervous and psychic

[7] STEINBERG, Isidoro R. & CRIVELLARI, C. A. Accidentes post-vacunales antirrabicos dos casos. *Primer Congr. Nac. Enfermedades Endemo-Epidémicas, Buenos Aires, 1942, Nov. 9–13,* 469–71.

changes, Kernig's and Brudzinski's signs were positive, later there was paralysis of the lower limbs, and retention of urine requiring daily catheterization. The first symptoms were those of meningitis, but when paralysis of the lower limbs set in treatment was suspended. There was no hydrophobia and this led to the belief that it was not a case of rabies and the subsequent evolution of the condition confirmed this opinion.

The second case occurred 13 days after treatment commenced, there was nausea, vomiting, headache, epigastric pain, weakness of the lower limbs with difficulty in walking, cutaneous hyperaesthesia at the sites of paralysis. The reflexes were exaggerated and Babinski's sign of the right foot was positive. The abdominal and cutaneous reflexes were diminished, and the cremaster reflex abolished. There was retention of urine. There was almost complete recovery in about three weeks in both cases. The treatment, which may be described as symptomatic, included repose and administration of "serum glucosé," camphorated oil, vitamin B_1, and liver extract. In one case sulphanilamide was given. This was omitted in the other and leucotropin (a compound of methenamine and cinchophen stated to be for intravenous injection in inflammatory processes) was given. Since both patients recovered it is concluded that no specific action would be attributed to sulphanilamide.

Aujeszky's Disease.

LÉPINE, LEVADITI, GRABAR and GUINTINI[8] have attempted to estimate the size of the virus of Aujeszky's disease by the methods of ultrafiltration and ultracentrifugation with a view to studying the technique and comparing the results. [The size of this virus had already been estimated by the method of ultrafiltration by ELFORD and GALLOWAY in 1936 as 100 to 150 mμ [this *Bulletin*, 1937, v. 34, 232]; these authors studied two strains of virus: one a strain, A.P., recovered originally from dogs in Hungary and subsequently passaged in rabbits, which was sent to the reviewer in 1930 by AUJESZKY, and the other a strain, M.I., recovered from cattle in America and subsequently passaged in rabbits, which was sent to the reviewer for study in 1932 by SHOPE.]

The present authors employed a strain which was apparently one of those recovered from cattle in France in 1936 by CRUVEILHIER, TRUCHE and VIALA [this *Bulletin*, 1936, v. 33, 746]. The brains of cats or rabbits infected with the disease were used as the source of virus, and guineapigs and cats as test animals for the infectivity of ultrafiltrates and centrifugates. Their ultrafiltration methods were based on those employed by the previous investigators and their estimate of 100 to 112 mμ agrees quite well with that already recorded. The size estimated by ultracentrifugation, while employing the inverted capillary tube method and Elford's formula (for technique see LÉPINE, *Ann. Inst. Pasteur*, 1941, v. 67, 380), was 68 to 100 mμ according to whether the assumed density of the virus particle was taken as 1·3 (nucleo-protein) or 1·16 (vaccinia). The sedimentation constant is given as $8{\cdot}8 \times 10^{-11}$. [In criticism, in view of the restricted number of animals used in the tests and perhaps also because the less

[8] LÉPINE, P., LEVADITI, Jean C., GRABAR, P. & GIUNTINI, J, Ultrafiltration et ultracentrifugation comparées du virus de la maladie d'Aujeszky. *Ann. Inst. Pasteur.* 1943, July–Aug., v. 69, Nos. 7–8, 238–41.

sensitive guineapig was employed (it is noteworthy that ELFORD and GALLOWAY's stock filtrates had a titre of 10^{-5} in rabbits, whereas the present authors record titres in guineapigs of 10^{-2}), the conditions of centrifugation just sufficient to ensure

$$\frac{C_t}{C_o} = \frac{\text{Average concentration after spinning for time t}}{\text{Concentration in original unspun control}} = 0{\cdot}1$$

does not appear to have been determined with sufficient accuracy. This may account for the lower figure given by this method of estimation when as a rule the tendency is in the opposite direction, *i.e.* the estimate by ultrafiltration is slightly lower. The authors state that, contrary to the opinion of REMLINGER and BAILLY, they found the guineapig to be more sensitive than the cat ; however, the observations are very limited in number.]

The authors conclude that in view of the experimental difficulties the two estimations should be considered as being in fairly good agreement. *Ian A. Galloway.*

LEVINSON, S. O., MILZER, A., SHAUGHNESSY, H. J., NEAL, J. L. & OPPENHEIMER, F. **Production of Potent Inactivated Vaccines with Ultraviolet Irradiation. II. An Abbreviated Preliminary Report on Sterilization of Bacteria and Immunization with Rabies and St. Louis Encephalitis Vaccines.** *J. Amer. Med. Ass.* 1944, June 24, v. 125, No. 8, 531–2. [10 refs.]

The inactivating effect of ultraviolet light on bacteria and viruses was investigated by exposing continuously-flowing thin films of infective suspensions to the rays of a specially designed lamp. Suspensions of *Bact. coli*, *Bact. typhosum*, *Bact. enteritidis*, *Staph. aureus*, *Strep. viridans* and *Strep. pneumoniae*, containing 10,000 million organisms per cc., were completely sterilized after an exposure of 0·33 second. Inactivation of the S–1 strain of fixed rabies virus in the form of a 4 per cent. brain emulsion was obtained with a similar exposure ; when used as a vaccine the irradiated virus produced a considerably higher degree of immunity than standard phenolized vaccines, and no significant loss of antigenicity occurred after storage at 5°C. for six months.

Up to 0·66 sec. exposure was necessary to inactivate the virus of St. Louis encephalitis in the form of a 4 per cent. brain emulsion ; vaccine prepared from irradiated virus produced a high degree of immunity in mice. *D. J. Bauer.*

MALARIA.

WYNTER-BLYTH, M. A. **A Note on the Transmission of Malaria at Ketti, Nilgiris, 6,300 Feet.** *J. Bombay Nat. Hist. Soc.* 1943, v. 44, No. 2, 307–9. [Summary taken from *Rev. Applied Entom.* Ser. B. 1944, July, v. 32, Pt. 7, 144.]

Malaria is not usually transmitted in the Nilgiris at altitudes of more than 4,000 ft. P. F. Russell explained an outbreak that occurred in September 1941, at an altitude of 6,300 ft. in the valley of Ketti, by the fact that over 2,000 labourers were brought during the year into

a place 2–3 miles away, many of them from malarious districts. This might account for the outbreak in question, but not for a few cases that the author records as having occurred in earlier years. He suggests that the easterly and north-easterly winds that prevail, respectively, just before and just after the south-west monsoon, the periods at which the cases of malaria occurred, enter the valley from the malarious plain and reach Ketti as a southerly breeze, encouraging mosquitos normally found at low altitudes to ascend the valley. When these winds are blowing, it is protected, warm, damp and marshy and would therefore favour Anopheline breeding.

SCHIAVI, A. Um caso de quartã registrado pelo nosso Serviço em Jupiá. [**A Case of Quartan Malaria registered in Jupiá.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 201–2. English summary.

"The author refers to another case of infection determined by *Plasmodium malariae* in Jupiá district (State of S. Paulo, Brazil) and registered by Service of Prevention of Malaria, of S. Paulo Health Department. He relates that only eight cases of malaria engendered by this species of plasmodium have been up to 1943 registered in the State of S. Paulo."

DE MELO, V. H. Um caso autóctone de malária quartã no municipio de José Bonifacio, Estado de S. Paulo. [**A Case of Quartan Malaria in the State of São Paulo.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 205–7.

DE MELO, V. H. Um caso autóctone de malária quartã no municipio de Porto Feliz, Estado de São Paulo. [**A Case of Quartan Malaria in the State of São Paulo.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 211–12, 5 figs.

CÔDA, D. Um caso de malária quartã no litoral Sul. [**A Case of Quartan Malaria in the State of São Paulo.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 215–16.

UNTI, Q. Novas concepções sobre o ciclo evolutivo dos plasmodidae. [**New Conceptions as to Developmental Cycle of Plasmodia.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 175–80, 1 fig.

The author traces the development of the modern conception of malaria as starting from the sporozoites' invasion of cells of the reticulo-endothelial system and the subsequent infection of the red blood corpuscles. The stages in the reticulo-endothelial cells are responsible for development during the incubation period and for later relapses of the blood infections which occur at varying intervals. [The article is a useful historical summary but it contains no new information, unless the author's view that malaria is primarily an infection of the reticulo-endothelial system, and only secondarily a blood infection, be regarded as such.] *C. M. Wenyon.*

AUSTRALIAN MILITARY FORCES. **Notes on Malaria for Medical Entomologists, 1943.** 20 pp., 6 figs. Notified in G.O.'s dated 30th June, 1943. L.H.Q., 1943. By Authority: Arbuckle Waddell Pty. Ltd., 20 McKillop St., Melbourne.

This is an admirably clear and concise description of the natural history of malaria, adequately illustrated. The notes were designed for the benefit of medical entomologists engaged on anti-malaria work. They contain much that is not of direct concern to the entomologist as such but nothing that is not essential to an appreciation of the importance and significance of the entomological side of malaria control. As an introduction to the study of malaria the pamphlet should be of great value to a much wider range of students than its title indicates.

Norman White.

KALANDADZE, L. P. & SAGATELOVA, I. S. [**Effect of Dry and Moist Substrata on the Viability of Mosquito Eggs.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 2, 24–31, 2 figs. [In Russian.]

After water collections have been dried in the course of anti-larval operations they are liable to be gradually refilled with water (by rain or irrigation), with the result that they are repopulated by mosquitoes developing from eggs or larvae that have survived at the bottom.

In order to elucidate the conditions under which this takes place, the authors have studied the effect of dry and moist substrata upon the viability of mosquito eggs, under laboratory conditions. In the experiments on the effect of dryness, the eggs of *Anopheles maculipennis maculipennis* were removed from water and placed in crucibles (20 in each) containing dry earth, sand, plants, etc. In the experiments on the effect of moist substrata, batches of 20 eggs each were placed on earth mixed with varying proportions of water, the test-vessels (100 cc.) being kept in a special apparatus in which the desired amount of moisture could be automatically controlled. In both sets of experiments, after exposure for various periods of time, the vessels were filled with water. The eggs were then allowed to hatch and the larvae were left to complete their development. Similar experiments were carried out with *A. bifurcatus* and *Culex pipiens.*

It was found that the degree of resistance to desiccation in *A. maculipennis* depended on the stage of development attained by the embryo; if this was far advanced the eggs remained viable after exposure on completely dry substrata for 26–29 hours (at 27·6–26·5°C.). The eggs of the anophelines proved to be more resistant than those of the culicine mosquitoes. The viability of eggs kept on moist substrata (humidity 33·3 per cent.) was considerably greater than that of eggs kept on dry substrata. Thus, the eggs of *A. maculipennis* survived on moist earth for 7 days at 21·5°C., as compared with a maximum of 29 hours on dry earth. In experiments conducted under natural conditions it was shown that the period of survival of the eggs depends upon the amount of moisture present in the soil and on the rate of its drying.

It is concluded that the drying of water collections can only be effective as an anti-larval measure if it is complete, since in the presence of the slightest amount of moisture in the bed mosquito eggs can survive for over a week and hatch later if inundated with rain water.

C. A. Hoare.

JUKOV, N. M. & KRASIKOVA, V. I. [**Epidemiological Rôle of** *Anopheles maculipennis messeae* **hibernating in the Houses in Siberia.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1942, v. 11, No. 5, 35–8, 2 figs. [In Russian.]

The authors note that in 62 out of 150 houses (42 per cent.) of a village in Siberia, mosquitoes (*A. maculipennis messeae*) hibernate in cellars which communicate with the living quarters by means of a trap-door in the floor, through which the insects find their way into the rooms. The winter temperature in the cellars—which are used for storing food, etc.—varies from 3·4 to 7·1°C. Mosquitoes have been captured in these houses from December to April, mostly during twilight. It was found that the percentage of mosquitoes containing blood gradually rose from 5·4 in December to 28·1 in April, during which period there was also an increasing number of females with ovaries in the 5th phase of development, *i.e.* ready to lay eggs. It was demonstrated that the mosquitoes laid eggs in the moist soil of flower pots which were kept in the house. The dissection of 1,080 mosquitoes captured during the winter months revealed one with sporozoites in the salivary glands, while under experimental conditions 40·2 per cent. of mosquitoes (77), fed in March on a patient harbouring gametocytes, became infected.

It was thus shown, (1) that in the presence of suitable human cases mosquitoes hibernating in Siberian houses may become infected, and (2) that the parasites are capable of completing their development in the vector. House-infections are therefore of epidemiological importance in Siberia and should be checked by destroying the mosquitoes in the houses after the outside windows of the cellars have been closed for the winter. *C. A. Hoare.*

SABROSKY, C. W. **A Malaria Mosquito Survey of Southern Michigan.** *J. Econom. Entom.* 1944, Apr., v. 37, No. 2, 312–13.

UNTI, O. & RAMOS, A. S. Sobre a fauna anofélica do vale do Paraíba (Diptera-Culicidae). [**The Anopheles of Paraíba.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 23–34, 5 figs. [15 refs.]

GALVÃO, A. L. A., LANE, J. & UNTI, O. Sobre o *Anopheles noroestensis* Galvão e Lane, 1938. *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 37–48, 6 figs. [10 refs.] English summary.

RAMOS, A. S. Observações sobre os anofelinos do litoral paulista. *Anopheles* (*Nyssorhynchus*) *tarsimaculatus* (Goeldi, 1905), *Anopheles* (*Nyssorhynchus*) *oswaldoi* Peryassú, 1922). [**The Anopheles of the Coast of São Paulo :** *A. tarsimaculatus* **and** *A. oswaldoi.*] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 51–62, 8 figs. [21 refs.] English summary (8 lines).

GALVÃO, A. L. A. Chaves para a determinação das espécies do subgênero *Nyssorhynchus* do Brasil. [**Key to Species of the Subgenus** *Nyssorhynchus* **in Brazil.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1943, Sept., v. 8, No. 19, 141–62, 34 figs. [48 refs.] English summary.

DENHOFF, E. & PIPER, B. C. **Laboratory Aids in the Diagnosis of Malaria.** *J. Lab. & Clin. Med.* 1944, May, v. 29, No. 5, 518–24, 1 fig. [10 refs.]

The authors describe the methods they use in the diagnosis of malaria in an Army Hospital operating in the south and south-west Pacific. The first year of practising what they call "jungle medicine" was a trial and error period for others, as well as themselves, who had not previously had much experience in the laboratory diagnosis of tropical diseases.

A description of the technique employed in finding malaria parasites follows.

It is stressed that the finding of parasites, pigmented leucocytes and a high percentage of monocytes in the blood smear are the chief considerations in diagnosing malaria. Troops who are taking regular suppressive atebrin complicate the diagnosis because in less than 40 per cent. will parasites be found (at least in the initial smear), and even then many of the parasites will be atypical in appearance. Because of this the authors stress the importance of searching for parasites in thick films, but they point out that for species diagnosis, thin films should also be examined. Blood films should be taken before treatment is started, but this is not intended to imply that treatment should be withheld until after malaria has been diagnosed microscopically. The authors advocate repeated blood film examination at intervals of 4–8 hours in patients who are receiving suppressive therapy. [Presumably this is for malignant tertian cases only.]

In their experience, parasites are generally found before the sixth film is taken, usually in thick smears. Parasites may be difficult to find when large doses of atebrin or quinine have been given twelve hours previously.

A thick film is prepared by placing a small drop of blood towards one end of a slide and spreading it so that the hands of a watch can just be seen through the blood. A thin film is prepared at the opposite end of the slide, which is then placed in a semi-vertical position to dry; the excess blood from the thick smear is allowed to drain down the slide to a heavy crayon mark previously prepared about ¾ inch from the end of the slide. In damp weather the film is dried in a hot air chamber. Thick films are stained by Field's method [this *Bulletin*, 1942, v. 39, 17].

Thin films are stained with a combination of Wright's and Giemsa's stain. Fourteen to sixteen drops of Wright's stain are floated on the centre of the thin film and allowed to stand for ½–1 minute; this is then diluted with 24–26 drops of distilled water, buffered to a *p*H of 7·0. The mixture is allowed to act for about ten minutes, and the film is then well washed with water. It is then decolourized with 95 per cent. ethyl alcohol and again stained; this time with Giemsa diluted with 15 parts of buffered distilled water, for about 30 minutes, when it is washed, dried and examined.

The parasites of all three species, as seen in thick and thin films, are described.

Among other laboratory aids mentioned is the fact that in some cases, 20 per cent. of the white cells may contain malarial pigment. The blood of patients with cerebral malaria should be typed upon admission to hospital and a blood transfusion given at the first indication of rapid blood destruction.

[There is much in this article with which to disagree. There is no apparent advantage in sloping the slide containing the thick drop of blood. With practice a drop of blood can be so arranged that the depth is greatest in the centre and less towards the periphery. A thick film which is moved about or is in motion for some time before drying is liable to peel off the slide during staining with a watery stain; probably the heat used in drying the films helped to prevent this.

The method advocated for staining thin films is not to be recommended. One suspects that the authors were unfortunate in the brand of Wright's stain supplied. Furthermore, the quantity of stain used for each thin film is extremely wasteful and must entail much care to prevent such a large quantity (2½ to 3 cc.) of stain mixture per slide from spilling over the slide. If a good brand of Leishman or Wright stain is used, four drops of stain and treble the quantity of distilled water should give excellent results, but the distilled water should be either neutral or very slightly alkaline, *p*H 7·2.

Ten to fifteen seconds with the stain alone is sufficient for fixing, but in hot weather four drops of stain evaporate quickly and it is advisable to fix the film first in alcohol for a few seconds, dry it and stain; then even five seconds with the stain before diluting suffices, followed by ten minutes staining with the mixture, excellent results being obtained. If Leishman's or Wright's stain is working properly it should not be necessary to restain with Giemsa or any other stain.

The authors advise that patients with cerebral malaria should be given a blood transfusion when there is an indication of rapid blood destruction. It would have been worth stating that the donor should be free of malaria, so that a fresh infection may be avoided.]

P. G. Shute.

PUHLMANN, H. Ueber rudimentäre Malariaerkrankungen in den Wintermonaten. [**Rudimentary Malaria in Winter.**] *Deut. med. Woch.* 1944, Feb. 4, v. 70, No. 5/6, 64–6, 2 figs.

In the case of various mild complaints, particularly in the autumn or winter months, patients who have had or been exposed to malarial infections may, without having actual attacks of malaria, show slight rises of temperature associated with severe headache. These may be isolated rises once every two weeks, or continued fever over a period up to ten days or a fortnight. The examination of three or four thick films of the blood may be necessary before a malarial parasite can be found and an explanation given. There is little else to guide one to a diagnosis of the condition, which is best treated by a combination of atebrin and plasmoquine. The parasite responsible is usually that of benign tertian malaria but occasionally the malignant tertian form is found.

C. M. Wenyon.

RENIGER-ARESHEVA, M. L. **Vitamin C in the Placenta and in the Foetal Organs in Malaria.** 7 typed pp., 2 pls. [From the Clinic of Puerperal Infections of the Institute of Obstetrics and Gynaecology of the Armenian S.S.R.]

The author, during many years of study of the pathology of pregnancy in malaria, has observed manifestations suggestive of scurvy in a number of serious cases. This condition of hypovitaminosis C is regarded as being provoked by the malarial condition and aggravated

by the pregnancy; the author has studied it by estimating the concentration of vitamin C in the placenta and in the organs of the foetus, and by comparison with normal controls. Estimations were made by Tilman's method as modified by Harris and Ray.

Tables are given which show that in the spring there is a deficit of 0·38–0·98 mgm. per cent. in the vitamin C content of the placentas of women suffering from malaria, in comparison with healthy women on the same kind of diet. In summer and autumn the average vitamin C content is higher, especially in the controls, but the difference between malaria and control patients may be as much as 7·15 mgm. per cent. An over-all average shows that the vitamin C content in malaria was 3·45 mgm. per cent.; in healthy women 13·51 mgm. per cent. In the tissues of the foetus there is a similar diminution in malaria. In the tissues of pregnant women who have died of *Plasmodium falciparum* infections the vitamin C content is very low. The more severe the malaria the greater is the reduction of vitamin C in all these tissues.

Vitamin C excretion in the urine was also investigated. It is known that this is reduced in pregnancy, on a normal diet; in pregnant women with malaria the average of 13·7 mgm. per cent. is compared with the 27·5–41·9 mgm. of normal persons.

In the opinion of the author, such manifestations as petechiae, stomatitis, gangrene of parts of the skin, and abortion in malaria, cannot be explained by the action of the malarial toxin alone; the rôle of hypovitaminosis C must also be considered in these processes.

Charles Wilcocks.

SCOTT, J. G. **Herpes Simplex Corneae in Malaria.** [Memoranda.] *Brit. Med. J.* 1944, Aug. 12, 213.

Four cases (in three patients) of herpes simplex corneae occurred in a series of 4,000 cases of malignant malaria in Europeans in West Africa. The clinical diagnosis of malignant malaria was confirmed microscopically (ring forms) in 35 per cent. of the cases. [It is not stated whether malarial parasites were found in the three patients with herpes of the cornea.]

Case 1.—Herpes appeared on the lip on the 2nd day and on the right cornea on the 8th day. Staining showed multiple fissures in the corneal epithelium; corneal sensitivity was diminished. Recovery took place in 10 days, leaving one nebula. After another (the third) attack of malaria, two months later, the nebula had faded and sensitivity was normal.

Cases 2 and 3.—The patient had herpes simplex corneae during the first and fourth of 5 malarial attacks, and had herpes labialis in the 5th attack. On both occasions a dendritic ulcer of the cornea developed. The first herpes appeared on the 16th day, in the left eye, and healed, under treatment with atropine and heat, in 40 days, leaving a scar. The second herpes appeared on the 7th day, the dendritic ulcer developing on the old scar. The whole corneal epithelium was removed with an alcoholic solution of iodine, 7 per cent., and potassium iodide, 5 per cent., and recovery was obtained in 10 days, leaving the old scar, and impaired sensitivity. No eye complication developed in another attack of malaria which occurred 3 months later though the corneal sensitivity was still impaired. The original corneal scar was then less pronounced.

Case 4.—Herpes of the cornea appeared on the 10th day; a small ulcer formed near the limbus and was slow to heal. Under treatment with atropine and heat it healed in 5 weeks.

The author states, in comment, that the best results followed removal of the corneal epithelium with strong iodine solution. *J. F. Corson.*

FENTON-RUSSELL, D. **Cerebral Malaria.** [Correspondence.] *Brit. Med. J.* 1944, June 24, 854.

The writer of this letter believes that too much emphasis is placed upon the more severe types of cerebral malaria, since in his experience in the far East the milder types were more frequent. It was not uncommon to find a soldier accused of being drunk and disorderly, or absent from his unit, to be suffering from cerebral malaria. Many cases of impulsive violence in the Far East have been caused by quartan cerebral infection.

In treatment, local experience is a good guide—3 to 10 grains of quinine may be given intravenously, but, as quinine abscesses are by no means rare, the author cannot recommend intramuscular injection. He believes that a course of psychotherapy should be given in all cases of cerebral malaria; if this were done, some of the tragedies which follow the disease could be avoided. *Charles Wilcocks.*

GAVAN DUFFY, C. A. **Report of a Case of Cerebral Malaria.** *Indian Med. Gaz.* 1944, May, v. 79, No. 5, 211.

ROGAN, J. M. **Treatment of Cerebral Malaria.** [Memoranda.] *Brit. Med. J.* 1944, Aug. 5, 181.

The author refers to recent reports of cases of cerebral malaria and in particular to one by SNEDDON [this *Bulletin*, 1944, v. 41, 259] in which he considers the commentary on treatment to be seriously misleading. Various courses of treatment of cerebral malaria have been recommended in recent years by authors with much experience of the condition; these are given in tabular form. Since the outbreak of the present war, however, exceptional opportunities have occurred for the study of the disease and the author gives the following directions as representing the most recent recommendations of the Allied Forces.

Quinine dihydrochloride, 6–10 grains, should be given intravenously very slowly—not exceeding 1 grain per minute and best at the rate of 1 grain in 2–4 minutes. The dose is dissolved in 10–20 cc. of distilled water or normal saline (normal saline-glucose for larger quantities). Subsequently, 6 grains are given i.v. every 4–6 hours, or 10 grains 8-hourly, up to a maximum of 30 grains in 24 hours, until recovery from coma occurs and satisfactory oral administration becomes possible.

Even when the prognosis appears hopeless, intravenous administration of quinine should be continued; in a case reported by WHITEHILL [this *Bulletin*, 1944, v. 41, 450] recovery took place after coma had lasted for over 3 days.

The author states that pulmonary oedema is a not uncommon terminal event in cerebral malaria and suggests that fluid [for the correction of dehydration] should be given through a Ryle's tube introduced into the stomach and connected to a drip apparatus, as recommended to him by Lieut. Col. G. A. RANSOME, I.A.M.C., rather than by a large intravenous infusion.

Other details, mentioned as being important, are a semi-recumbent posture for the patient and the performance of lumbar puncture as a

routine procedure in all cases of coma; this may disclose a high c.s.f. pressure or concomitant cerebrospinal meningitis. [For other recent papers on cerebral malaria see this *Bulletin*, 1944, v. 41, 6, 358, 450 and 538.] *J. F. Corson.*

KONJ, J. S. & YAKOVLEVA, O. I. [**The Effectiveness of the Prolonged Course of Anti-relapse Malaria Treatment.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1942, v. 11, No. 5, 20–24. [In Russian.]

This work was carried out in an area of central Russia covered by the Lenin Railway net, where the spring relapses of malaria constitute 25–30 per cent. of the total number of attendances for this disease in the course of the year. In this region benign tertian malaria was predominant (91·2 per cent.), subtertian being responsible for only 8·8 per cent. of cases. The authors point out that the method of treatment against relapses advocated by the Commissariat of Health (a course of 31 days in 3 cycles) was inadequate, since after such treatment the number of relapses still amounted to 21 per cent. With a view to reducing this figure, the authors have introduced a course of prolonged treatment, to cover the entire period during which relapses usually occur (April–June), as shown in the following table:—

Drug	Daily dose in gm.	Days when administered
Acriquine	0·2	1, 2, 3, 4, 5–10 days' interval
,, ...	0·2	16, 17, 18–10 days' interval
,, ...	0·2	29, 30, 31–10 days' interval
Acriquine + Plasmocide ...	0·2 0·04	42, 43, 44–10 days' interval
,, ,, ,, ...	[0·2]* 0·04	55, 56, 57–10 days' interval

[Acriquine is the equivalent of mepacrine, plasmocide is the equivalent of pamaquin.]

* No dose of acriquine is shown in the original paper; it is presumed that 0·2 gm. was given.

The authors' course of treatment (5 cycles in 57 days) was applied in March 1938 to 1,016 cases, the results being assessed in April of 1939 and 1940. These cases were compared with 632 patients who had been treated according to the government scheme (3-cycle course of 31 days), on the one hand, and with a control group of 191 persons who had received no anti-relapse treatment at all, on the other hand. It was found that the number of relapses in the first group was considerably lower than in the second and third, especially during the first four weeks after treatment (2·1, 18·8 and 41–48 per cent. respectively).

In view of the superiority of the prolonged anti-relapse course of treatment, it was repeated in the same locality in 1940. Eleven months later only 6·8 per cent. of the patients relapsed, whereas in another community, where the 31-day course was retained, the percentage of relapses remained unchanged. The effectiveness of the prolonged method of treatment was also reflected in a diminution of the number of working days lost owing to malaria. *C. A. Hoare.*

JOHNSON, F. H. & SCHNEYER, L. **The Quinine Inhibition of Bacterial Luminescence.** *Amer. J. Trop. Med.* 1944, May, v. 24, No. 3, 163–75, 9 figs. [28 refs.]

It is not yet certain how the cinchona alkaloids exert their effect on malaria parasites. Probably enzyme systems in the parasite are affected by combination of the drug with its protoplasmic constituents. To throw light on this question, the authors have investigated the inhibition produced by different concentrations of quinine on bacterial luminescence under varying conditions of temperature and pressure, as well as the reversible nature of the reaction and the effect of mixing quinine with other inhibitors. Essentially non-proliferating bacteria, *Photobacterium phosphoreum* and *Achromobacter fischeri*, were used, in which the emission of light is due to oxidation by molecular oxygen of a substrate (luciferin) by an enzyme (luciferase). The organisms were cultivated at their optimum temperatures, and emulsified in a phosphate-buffered salt solution. After aeration they were mixed with quinine in the desired concentration. The intensity of emitted light was measured by means of a photoelectric cell and amplifier. The enzyme may occur in active or inactive form and is capable of combining with drug or metabolic products. Two types of combination are possible between enzyme and drug, depending on the conditions accompanying the denaturation of the enzyme.

Addition of quinine to the cell suspensions caused a decrease of luminescence to a value which remained constant for a time and allowed of accurate comparison with the control. This inhibitory action of quinine involved a reversible combination between drug and enzyme, was not due to killing of some of the bacterial cells, and was practically independent of cell concentration at a given dilution. Analysis of the relationship between concentration of drug and inhibition of luminescence produced under constant conditions of temperature and pressure showed that 1 to 1·5 molecules of quinine combined with 1 molecule of enzyme.

The author concludes that the action of quinine is similar to that of other substances causing reversible denaturation of enzyme protein and the degree of inhibition is affected by temperature and pressure. He indulges in some speculation on the mechanism of quinine therapy, based on his experimental findings, and puts forward an explanation for the contrast in results of quinine treatment of different malarial parasites.

[This is a highly technical paper and will repay study by those interested.] *J. D. Fulton.*

KELSEY, F. E., GEILING, E. M. K., OLDHAM, F. K. & DEARBORN, E. H. **Studies on Antimalarial Drugs: the Preparation and Properties of a Metabolic Derivative of Quinine.** *J. Pharm. & Exper. Therap.* 1944, Apr., v. 80, No. 4, 391–2.

When quinine is incubated *in vitro* with various tissues it is converted into substances which no longer have the solubility or fluorescent characteristics of quinine. Apparently the livers of some species of animals are more active than others in this respect, and more than one modification of quinine is produced. After incubation of quinine with sheep liver, I. J. LIPKIN [this *Bulletin*, 1920, v. 15, 127] isolated quitenine, and after incubation with guineapig liver he isolated a second

product. Kelsey and his associates worked with rabbit liver and isolated yet a third product. For the method of isolation and the chemical properties of this new compound, the original should be consulted. Its formula and its relation to quinine have yet to be determined.

F. Hawking.

PICK, E. P. & HUNTER, J. **The Action of Atabrine on the Electro Cortico Potentials.** *J. Pharm. & Exper. Therap.* 1944, Apr., v. 80, No. 4, 354–61, 4 figs. [20 refs.]

If suitable electrodes are placed on the cerebral cortex, changes of electrical potential can be recorded. In lightly anaesthetized cats and in frogs the changes take the form of characteristic rhythmical waves. Cats were anaesthetized by nembutal and given mepacrine (atabrine) 5–12 mgm. per kgm. intraperitoneally or intravenously. The rapid wave frequency disappeared in 66 per cent. of the cats and only slow waves of low amplitude remained. This effect indicates a central depressant action of mepacrine. Usually it did not appear until one hour or longer after the intravenous injection of mepacrine, although sometimes it appeared within a few minutes; according to the dose given it persisted for 1 to 4 hours. Apparently it was related to the mepacrine content of the brain rather than to that of the blood.

Similar changes were seen in the electrocorticogram of pithed frogs following the injection of 0·5–1 mgm. mepacrine. Larger doses of mepacrine caused blockage of reflexes and finally paresis and death. It is recalled that mental disturbances occasionally follow the clinical administration of mepacrine [these mental disturbances are rare unless large doses are given; hyperexcitability is more common than depression]. It is believed that these changes in the electrocorticogram are another manifestion of the same action. *F. Hawking.*

GORGAS MEMORIAL LABORATORY ANNUAL REPORT, 1943 [CLARK, H. C., Director]. 4–14. **Experimental Work in Control of Malaria by Use of Drugs.**

This is a report of the 13th year's observations of the control of malaria by the use of drugs in the Panama Canal Zone. Since the last report four new conditions have been operative which might influence the malaria parasite index in the villages under observation. Copper sulphate has been widely used to kill aquatic vegetation along river banks and lagoon areas during the rainless months of the year. The health authorities have been using a high-powered paris green dusting apparatus over the same river area once a week. The impounded water of Madden Dam, above the observation villages, has been used at intervals to flush the aquatic vegetation from river and lagoon downstream. The chief anopheline breeding places for the observation villages are, however, in small branches of the river behind the villages; these have not been affected by any of the three measures. Lastly, villagers have returned after periods of employment outside sanitated areas, where they were housed in unscreened quarters, with a higher parasite index than when they left the villages under drug control.

The atebrin group of villages consisted of Santa Rosa, Guayabilito, Gatuncillo, Las Guacas and Agua Clara, quite close together on the banks of the Chagres River. The quinine group was composed of the inhabitants of New San Juan, approximately equal in number to the

combined population of the atebrin villages. New San Juan is on the Gatuncillo branch of the Chagres River. Bi-monthly thick blood film surveys were made of both groups. Persons harbouring parasites were given either atebrin 0·1 gm. thrice daily for 5 days, or 18 grains of quinine sulphate a day for 5 days.

The inhabitants of Rio Pescado and Mendoza with a small group from Los Azules formed the control population. These places are on the west side of Gatun Lake, the Chagres villages on the east. The control group was surveyed monthly. A list of persons harbouring parasites was given to the local village office and to the school teachers. Those whose names appeared on the list could obtain free quinine if they desired to take it. Most of the families used very little of the drug.

The average monthly parasite rates and the cumulative rates for the year of the various groups (not including relapses) were :—

	Rate	
	Monthly	Cumulative
Atebrin group	10·9	30·5
Quinine group	8·9	20·9
Control group (Rio Pescado)	25·6	45·7
Control group (Mendoza, in the hills)	4·6	11·8
Control group (Los Azules)	13·6	26·9

The coming and going among the populations constituted insuperable obstacles to complete surveys and complete treatment.

The species of parasites found in 135 persons with relapses were : *P. falciparum* 61·4, *P. vivax* 28·1 and *P. malariae* 10·3 per cent. The clinical relapse rates, in the quinine and atebrin supervised groups, for the various species of parasite were : *P. falciparum* 9·8, *P. vivax* 16·3 and *P. malariae* 17·6 per cent. The author remarks that " general opinion seems to underestimate the importance of relapse in *P. falciparum* infections."

Only one baby during the first year of life was found infected in the treated villages : it was infected elsewhere. The control village Rio Pescado had five infected babies and Mendoza two.

The malaria infection rates generally were a little lower than in the previous year. Malaria incidence in 1943 was below the average throughout the Caribbean and Isthmian regions. [For previous reports in this series see this *Bulletin*, 1944, v. 41, 9.] *Norman White.*

CLARK, H. C. **Recent Research in Prophylaxis and Treatment of Malaria. Report for 1942–1943.** *J. Nat. Malaria Soc.* Tallahassee, Fla. 1944, June, v. 3, No. 2, 85–94. [20 refs.]

RIBBANDS, C. R. **Camp-Siting in Malarious Districts of West Africa.** *J. Roy. Army Med. Corps.* 1944, Apr., v. 82, No. 4, 157–64, 2 figs.

Experimental work in West Africa, on which this paper is based, has shown that camp-siting is an anti-malaria measure of great importance even in areas where there are no anopheline-free districts. Whatever the anopheline density susceptible uninfected troops can remain free from infection if their camp be 5 miles away from the nearest infected human population, and the risk is but small at a distance

of 2 miles. If, however, anopheles are breeding between the village and the camp these distances should be increased to 8 and 3 miles.

If the camp form part of an existing community it should be remembered that the number of anophelines per person is inversely proportionate to the size of the community. The malaria risk is usually much greater in villages than in towns. If the complete removal of the infected native population be impracticable, as it generally is, partial removal is worse than useless, unless it be the removal of children, the richest reservoir of infection. If the camp and infected community are separated but within mosquito range the one from the other an increase in the size of the community will tend to reduce malaria transmission in the camp if the anopheline breeding places are nearer to the community than to the camp. If the breeding places are adjacent to the camp increased native population in the infected community enhances malaria risks in the camp.

When white troops and native troops have to be camped together in malarious districts, the native lines should be placed between the anopheline breeding places and the white lines; the native troops may serve as an efficient protective screen for the white troops.

If two sites equidistant from anopheline breeding ground be available, the higher should be chosen; altitude deters anophelines. Bush clearing near camps is not an effective measure of protection against either *A. gambiae* or *A. funestus*.

An appendix describes the palp markings characteristic of the common West African vectors, and another describes a simple method of determining the density of adult mosquito infestation.

Norman White.

HEWITT, R. I. **Recent Research in Avian and Simian Malaria.** *J. Nat. Malaria Soc.* Tallahassee, Fla., 1944, June, v. 3, No. 2, 95–109. [Numerous refs.]

BLACKWATER FEVER.

WILSON, T. E. **Blackwater Fever.** *Med. J. Australia.* 1943, Nov. 20, v. 2, No. 21, 414–18, 2 figs.

This is an account of two cases of blackwater fever; the patients were Australian soldiers who had almost certainly become infected with subtertian malaria in Papua (New Guinea), although no subtertian malarial parasites were found either in the blood or the bone marrow. In civilian life before the war they had travelled in malarious countries and had had several attacks of malaria. During their period of treatment in hospital, repeated differential cell counts of the bone marrow were made as well as other observations so far as local facilities permitted. The patients were given blood transfusions, intravenous infusions of 5 per cent. glucose-saline solution, and large amounts of fluid by mouth, including sodium citrate solution. The various laboratory observations and the records of fluid intake and output are shown in tables.

The first patient received a blood transfusion of 25 ounces of citrated blood on each of the first 3 days of treatment; 390 ounces of glucose-saline solution intravenously, and 502 ounces of fluid by mouth in the first 5 days. The output of urine during this period was 484 ounces,

the lowest daily amount being 67 ounces. His urine regained its normal colour on the 4th day and he was convalescent on the 18th day. A point of interest is that 7 days before blackwater appeared he had a severe attack of fever and began a five-day course of atebrin, 0·1 gm. t.i.d.; on the 6th day he felt abdominal pains and malaise and on the 7th day his urine became black.

The second patient had had several attacks of fever in Syria in 1941. He first went to Papua in August 1942 and had much fever during the 10 months before his admission to hospital, with this attack of blackwater fever, in July 1943. On admission he was ordered quinine 10 grains t.i.d., but after the third dose his urine became black. Numerous trophozoites of *Plasmodium vivax* were found in his blood, on one day only, the first day after admission. He was given eight blood transfusions (total 395 ounces) during the first 5 days, 202 ounces of glucose-saline solution in the first 6 days, and 1,266 ounces of other fluids by mouth during the first 12 days. The output of urine during the first 12 days was 1,863 ounces. The urine became of normal colour on the 8th day and he was convalescent by the 25th day.

In both cases the normoblast cells, of different stages of development, in the bone marrow increased in number considerably during the early days of the illness and gradually returned to normal after haemolysis had ceased.

The author suggests that blackwater fever is due to sensitivity produced not by quinine but by a by-product liberated from the parasites by an anti-malarial drug. *J. F. Corson.*

SINGH, I. & SINGH, I. **Treatment of Blackwater Fever.** *Indian Med. Gaz.* 1944, June, v. 79, No. 6, 256–8.

The authors treated 37 cases of blackwater fever. All the patients had had malaria (1–5 attacks) during the preceding 12 months, 34 with subtertian and 3 with benign tertian, but two of the latter had crescents in their blood. All except one, who was bedridden, were going about their work when the attack of blackwater occurred, but they were taking antimalarial drugs; 18 were taking quinine, 18 pamaquin, and 1 mepacrine. In one the attack took place in April, in all the others between October and March. Thirty-five were debilitated and two in apparently good health.

Haemolytic substances were found in the blood but "their presence was very transitory."

Treatment.—The authors emphasize the good effect produced by giving concentrated antivenene [unspecified] intravenously. They treated 36 patients with it and all recovered, while the remaining patient, for whom it was not available, died. They gave 20 cc., then 10 cc., four-hourly for 72 to 96 hours; no further haemolysis occurred. Other treatment included the administration of sodium citrate by mouth and i.v., glucose, with vitamin C, i.v., calcium gluconate, blood transfusion in three cases, the bloods being matched "under the high power of the microscope." The resulting anaemia and debility were treated with "Fersolate," vitamin B, vitamin C, crude liver extracts, cod liver oil, and a generous diet. No antimalarial drugs were given although subtertian parasites were still present after the haemolysis had ended.

J. F. Corson.

TRYPANOSOMIASIS.

VAN HOOF, L., HENRARD, C. & PEEL, E. **Pentamidine in the Prevention and Treatment of Trypanosomiasis.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Feb., v. 37, No. 4, 271–80.

The rate of disappearance of *Trypanosoma gambiense* from the blood after treatment with pentamidine (diamino diphenoxy-pentane) is slow. In guineapigs, treated with a single dose of 2–3 mgm. per kgm. the trypanosomes disappeared in 41–54 hours. In patients, treated with 2 mgm. per kgm., trypanosomes disappeared from the gland juice after 48–72 hours. After a single dose of 5 mgm. per kgm., infected guineapigs did not relapse ; after 2–3 mgm. per kgm. about half relapsed in 11–125 days ; after doses of 1·5 mgm. per kgm. or less, relapses occurred in 15–91 days [number of guineapigs used not given]. Tryparsamide-fast strains responded to pentamidine as well as other strains did. When repeated doses were given to guineapigs, 3 mgm. per kgm. was the largest dose tolerated, and not more than 2 injections should be given each week. The best results were obtained with 1–2 mgm. per kgm.

Two patients with early trypanosomiasis were treated. One was given 10 injections, each of 0·05–0·1 gm. (total 0·95 gm.) twice weekly, and was cured. The other received two injections of 0·1 gm. and three of 0·14 gm., but he showed intolerance, and treatment was continued with tryparsamide and suramin. These doses of pentamidine, calculated at 1–3 mgm. per kgm., were injected intramuscularly. Fourteen cases of advanced sleeping sickness with pathological changes in the cerebro-spinal fluid, were treated, without significant benefit ; in a few cases a combination of pentamidine, tryparsamide and suramin was more effective.

Twelve guineapigs were given a single dose of 2 mgm. per kgm., or three doses of this amount repeated during a period of a few days ; the guineapigs were then exposed to infection at repeated short intervals from the bites of infected tsetse flies or from injection of infected blood. Trypanosomes did not appear in the blood of the guineapigs until after periods of 22 to 327 days ; in many cases, they did not appear until after 100 days. [Unfortunately it is not clear in these experiments whether infection was actually prevented during these periods, or whether the results were due to a prolongation of the incubation period.] Apparently the drug has a prolonged action with a slow rate of elimination or excretion, similar to that of suramin.

Two volunteers were investigated. Bonkumu received 2 mgm. per kgm. on Aug. 9th, 1941, and Moya received 3 mgm. per kgm. on the same date. Infected tsetse flies were fed on them every 2–3 days, and frequent blood examinations and blood cultures for trypanosomes were made. Moya was found infected on June 1st, 1942, a blood culture was positive on June 6th and tsetse flies were infected from him on June 2nd. Bonkumu was found infected on Aug. 10th, 1942, blood culture was not positive until Aug. 27th, but tsetse flies were infected on Aug. 24th and 25th. The clinical course of these two infections was peculiar. Trypanosomes were scanty, blood cultures and tests for xenodiagnosis yielded negative results for long periods after the infection had first appeared and then disappeared and the temperature remained normal. No local reaction occurred at the site of injection. Both volunteers were cured with suramin. [Unfortunately no description is given of untreated volunteers being similarly exposed to

infection as controls; the results as set forth permit the alternative explanation that the strain or strains of trypanosomes used were only feebly pathogenic for man, infection occurring only rarely and being very mild when it did occur.] Infected tsetse flies, fed on animals treated with pentamidine, do not become disinfected; and the development of infection in the fly is not prevented by this means. Field trials are now being made on the prophylactic action of pentamidine. In villages containing 500 inhabitants in a heavily infected part of the Kwango district, half the people were given an intramuscular injection of 2–3 mgm. per kgm. Three months later no new case was found among those protected, while 2·5 per cent. new infections have been discovered among the controls. [FULTON (below) gives a different explanation to the observations here recorded; his paper should be consulted.] *F. Hawking.*

FULTON, J. D. **The Prophylactic Action of various Aromatic Diamidines in Trypanosomiases of Mice.** *Ann. Trop. Med. & Parasit.* 1944, Apr. 19, v. 38, No. 1, 78–84.

The following 4 : 4'diamidino-derivatives were tested:—diphenylethane, stilbene, monomethyl stilbene, dimethyl stilbene, 2-hydroxy stilbene, tolane, diphenyl ether, and diphenoxy-propane and -pentane. A single dose of half the maximum tolerated dose (0·5–1·0 mgm. per 20 gm. mouse) was injected into mice which were later inoculated after a suitable interval with light suspensions of *T. rhodesiense* or of *T. congolense*. With diphenyl ether there was no protection after one week; with diphenyl ethane and tolane the protection lasted 2–3 weeks. With the other compounds complete protection lasted 2–4 weeks. The prophylactic power of the drugs is proportional to the curative index. In mice not completely protected, the infection often ran a prolonged irregular course.

Fulton also comments on the experiments recorded by VAN HOOF *et al.* (above). Fulton has observed in his own experiments that if mice were treated with pentamidine and then inoculated at frequent intervals with *T. rhodesiense*, apparent protection was observed for periods up to 8–24 weeks. But this protection is due to immunization produced by the frequent injections of trypansosomes and not to the prophylactic action of the drug (after the first 2–4 weeks). He considers the protection observed by van Hoof *et al.* to be due to similar causes. *F. Hawking.*

NISSLE, A. Studien zum Problem der Pathogenität toxinfreier Mikroorganismen (Trypanosomen) und des Wirkungsmechanismus chemotherapeutischer Mittel (nach früheren Versuchen). [**Studies on the Pathogenicity of Trypanosomes and the Action of Chemotherapeutic Substances (Early Work).**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1943, Dec. 11, v. 104, No. 2/5, 274–82.

CHAGAS FILHO, C. Moléstia de Chagas no Brasil. [**Chagas's Disease in Brazil.**] *Ilustração Médica.* Rio de Janeiro. 1944, Apr., v. 10, No. 1, 31–4.

LEISHMANIASIS.

DEVINE, J. **Experiments on the Properties and Quantitative Determination of 4 : 4′-Diamidino Stilbene Dihydrochloride (Stilbamidine).** *Ann. Trop. Med. & Parasit.* 1944, Apr. 19, v. 38, No. 1, 35–45, 2 figs.

A colorimetric method of estimating the concentration of stilbamidine is described, which depends upon the development of a yellow colour with glyoxal. The depth of colour obtained is measured by a Hilger's "Spekker" absorptiometer. The test is as follows: "2 c.cm. of stilbamidine solution containing not more than 0·1 mgm. per c.cm. are mixed in a thin-walled test-tube with 1 ccm. of 10 per cent. glyoxal (B.D.H.) plus 2 ccm. of 3N NaOH and heated by immersing in a boiling-water bath for 30 seconds. The tube is removed, cooled under running water for a few seconds, then in melting ice for five minutes. Finally 5 c.cm. of 15N H_2SO_4 (60 c.cm. of concentrated acid diluted to 144 c.cm.) are added quickly with shaking, the tube is warmed slightly in the hand to prevent subsequent moisture condensation on the cell during reading, and the solution is transferred immediately to the absorptiometer cell for determination with no. 7 (dark blue) filters." Several important precautions are necessary to obtain a reliable result; for these the original paper must be consulted. This method measures down to 0·01 mgm. A spectrophotometric method, described by GOODWIN [this *Bulletin*, 1943, v. 40, 684] has a sensitivity of about the same amount.

By the use of these methods it is demonstrated that when a solution of stilbamidine is exposed to "good window light" for about two hours, two-thirds of the compound are transformed into a derivative which does not respond to these tests. After two hours a stable state is reached. For fuller details see FULTON and YORKE [this *Bulletin*, 1943, v. 40, 23], FULTON [*ibid.*, 683] and GOODWIN [*loc. cit.*]

According to BARBER, SLACK and WIEN [*ibid.*, 376] the chief product is 4 : 4′-diamidino-phenyl benzyl carbinol formed by hydration of the central double bond. Stilbamidine is relatively stable to light in the solid state. When dissolved in serum or plasma, stilbamidine can be quantitatively assayed by preliminary deproteinization with dialysed iron. [A simple method, described by HENRY and GRINDLEY (this *Bulletin*, 1943, v. 40, 122) can be used to measure concentrations of stilbamidine as low as 0·025 mgm. per 100 cc. in a few drops of fluid, but the accuracy is only about 50 per cent.] *F. Hawking.*

PRICE, F. L. & MAYER, R. A. **A Case of Kala-Azar.** *J. Amer. Med. Ass.* 1944, June 17, v. 125, No. 7, 490–92, 2 figs.

"1. In a case of kala-azar the diagnosis was made by finding Leishmania donovani organisms in smears of splenic pulp.

"2. Treatment with a pentavalent antimony compound brought about prompt clinical improvement.

"3. Treatment was complicated by an exacerbation of fever, abdominal pain and bloody diarrhea, which may or may not have been caused by the administration of neostibosan."

NATTAN-LARRIER, L., RONCHÈSE, A. D. & STEEG, L. Les infections expérimentales du Mérion par *Leishmania donovani*. [**Experimental Infections of the Vole with** *L. donovani*.] *Arch. Inst. Pasteur de Tunis*. 1942, Dec., v. 31, No. 3–4, 212–21.

Experimenting with the N. African vole (*Meriones shawi*) the authors have found that it is susceptible to infection with a canine strain of Mediterranean *L. donovani* isolated from a dog in Nice. The infection appears to follow inoculation with regularity but it is of a chronic character. In some cases it was proved that the young born of infected females were already infected at birth. It would seem that the vole is a more suitable animal for experimental work than the golden hamster of Palestine (*Cricetus auratus*) but less suitable than the spermophile (*Citellus citellus*) in which an infection runs a more rapid and regular course. *C. M. Wenyon.*

FEVERS OF THE TYPHUS GROUP.

GONZÁLEZ, E. Consideraciones sobre las reacciones biológicas en el diagnóstico del "Tifus exantemático" y especialmente en la fiebre tipo murino. [**Comments on the Biological Reactions in the Diagnosis of Exanthematic Typhus, especially of the Murine Type.**] *Gac. Med. de Caracas*. 1944, Apr. 15, v. 52, No. 7, 78–87.

The problem of the fevers of the typhus group in Venezuela is discussed.

Louse-borne typhus, locally known as "Guacarapa fever," "fevers of Caracas," etc., has been recorded in the State of Miranda and the Federal District from time to time between the years 1883 and 1931.

Typhus of a doubtful type has been reported from Bolivar State in 1921 and 1935.

Murine typhus has been reported since 1939 in Bolivar State and Caracas. In Caracas 31 among 500 rats examined had positive Weil-Felix reactions, all but one at titres of 1–50 to 1–100.

The author asks whether historic typhus has disappeared from Venezuela, and if so—why? *John W. D. Megaw.*

SPAET, G. **Investigations into the Aetiology of Exanthematic Typhus.** *J. Trop. Med. & Hyg.* 1944, June-July, v. 47, No. 3, 28–30.

In this paper, freely translated by Sir John Megaw, K.C.I.E., the author records his work at the Institute of Bacteriology of Chile; this work was a continuation of his earlier investigations in Prague (*Med. Klin.*, 1934, v. 30, No. 42, 1395) on typhus fever in experimentally infected guineapigs. These experiments led him to conclude that failure to cultivate the organism on cell-free media was due to the presence of anti-bacterial substances in the blood. In Santiago the author made lumbar punctures on a number of patients who had severe meningitic symptoms. He added the cerebrospinal fluid, in 10 cc. amounts, to large flasks containing 150–200 cc. of Levinthal's medium and obtained an abundant growth of small, slender, bacilliform organisms closely resembling Rickettsiae. These organisms were at first highly virulent to guineapigs but in the course of successive passages the virulence diminished and was finally lost.

In 1942, during a small epidemic of mild typhus, the author again tried to obtain cultures from the cerebrospinal fluid of patients, but the results were negative. Guineapigs were inoculated with the blood of these patients and did not show a febrile reaction before the 20th or 22nd day, resembling in this respect the results of the inoculation of the author's attenuated cultures. Three guineapigs died and showed, *post mortem*, inflammatory lesions of the typhus type. It was not possible to test the surviving guineapigs for immunity owing to the sudden ending of the epidemic ; the author therefore asks other workers to complete the investigation by carrying out immunity tests.

J. F. Corson.

RAETTIG, H. Die Blutsenkung bei Fleckfieber. Ein Beitrag zur Frühdiagnose. [**The Blood-Sedimentation Rate in Typhus Fever. A Help to Early Diagnosis.**] *Deut. Militärarzt.* 1944, Jan., v. 9, No. 1, 5–7, 3 figs.

Curves showing the average increase in the Westergren erythrocyte-sedimentation rate in typhus fever indicate that the rise is much slower and less pronounced than in other severe infections.

For example, the average rate in a large number of cases of typhus fever on the fifth day was about 15 mm. after one hour, as contrasted with about 80 mm. on the same day in cases of pneumonia. In some cases of typhus there was actually a fall in the rate ; usually there was a gradual rise reaching a maximum of about 30 mm., on the average, by the 17th day. On the same day in the pneumonia series the reading averaged 125 mm.

The great variations of the sedimentation rate in typhus were not related to the severity of the attacks or to the occurrence of complications ; in one mild case the highest reading after one hour was 6, in another it was 77. In one very severe case with bronchopneumonia it was only 7. In another severe case with bronchitis it rose to 62.

A relatively slow and moderate rise in the sedimentation rate is regarded by the author as an important clue to the diagnosis, especially in the early stages before the appearance of the rash or the occurrence of positive Weil-Felix reaction. So also a rapid rise to a high level is strong evidence that the patient is not suffering from typhus fever.

John W. D. Megaw.

KUHLMANN, F. & HEINRICH, K. Ueber Kreislaufstörungen beim Fleckfieber. [**Circulatory Disturbances in Typhus Fever.**] *Deut. Militärarzt.* 1943, Dec., v. 8, No. 12, 679–83, 6 figs.

This note deals with the cardio-vascular lesions in a group of 20 patients aged 20 to 42 years.

Electrocardiograms often showed an increase in the length of the P–Q interval towards the end of the febrile stage and early in convalescence. An appreciable increase in the Q-T interval towards the end of the fever was observed in all but two of the cases. The T wave showed progressive flattening, sometimes also a tendency to be biphasic or to show a negative after-wave ; this condition was most pronounced one or two days after defervescence. The normal condition was reached by the end of the fourth week of convalescence except in cases complicated by nephritis, though in some cases there was still evidence of myocardial damage up to the sixth or eighth week.

The association of indications of damage to the central nervous system with vascular lesions is discussed, with special reference to the localization of the lesions.

In some cases there was an extreme lowering of the diastolic blood pressure towards the end of the fever, and even in early convalescence; this often yielded to strychnine.

The necessity for avoidance of effort during convalescence is emphasized. *John W. D. Megaw.*

SEIFERTH, L. B. Ueber die Störungen des Hör- und Gleichgewichtsapparates und ueber die entzündlichen. Ohrerkrankungen beim Fleckfieber. [**Disorders of Hearing and Equilibrium; and Inflammatory Diseases of the Ear in Typhus Fever.**] *Deut. med. Woch.* 1944, Jan. 21, v. 70, No. 3/4, 23–4.

The investigations described in this paper were carried out in field-service conditions.

The first symptom of ear trouble is tinnitus; this is soon followed by giddiness and partial deafness. Patients who were sufficiently conscious to recollect what happened said that the symptoms appeared on the second or third day.

About 80 per cent. of all the typhus patients had ear symptoms; and in 73 of 80 patients with deafness this was regarded as being due to a central lesion. Four of the other cases were associated with an increased pressure of the cerebrospinal fluid, and three with internal-ear trouble which started in the third week.

The prognosis in cases of ear trouble was good on the whole, but the author had no personal experience of what happened later in cases in which the complications appeared late in the illness.

No less than 15 per cent. of all the typhus patients had suppuration of the middle ear, which usually began in the third week, and in some cases was profuse.

In 32 cases mastoid operation was needed; the results were good, except that one patient died of otogenic meningitis.

The prevailing organisms were haemolytic streptococci, and staphylococci.

Pilocarpine was employed with success in the treatment of the early manifestations of ear trouble, and lumbar puncture was valuable in cases with high pressure of the cerebrospinal fluid.

Otherwise the treatment of the ear complications was on the usual lines. *John W. D. Megaw.*

WOLMAN, M. **Treatment of Typhus with Anti-Typhus Horse Serum.** *Lancet.* 1944, Aug. 12, 210–12.

The anti-typhus serum was prepared from two healthy horses which had been immunized by injections of increasing doses of living Rickettsiae from the intestines of infected lice. The injections were given at five- to six-day intervals over a period of two and a half months. The horses were then bled twice—five and ten days after the last injection, respectively. In each subsequent month the horses were given a further course of three injections consisting of 250, 375, and 500 louse intestines, and two further bleedings were made.

The blood was collected in large sterile bottles to which a 5 per cent. solution of sodium citrate had been added to the amount of one-tenth of their capacity. The serum was siphoned off and preserved with merthiolate or phenol.

Alternate cases to the number of 220 were treated, and there were 220 untreated controls. The doses were of 20 cc. each; they were given subcutaneously, two on the first day of treatment and one on each of the following three days.

The relevant data are shown in the table.

		Treated	Untreated
Chief complications observed	Malaria	44	47
	Relapsing fever	7	7
	Lobar pneumonia	7	11
	Bronchitis	11	14
Duration of fever		11·99	13·25
Psychoses		5	17
Deaths		8 (=3·6 per cent.	24 (=10·9 per cent.)

Among 77 cases in which treatment was started on or before the 6th day there was no death. There were only four serum reactions; one of these was "quite serious." Abscesses occurred at the site of injection in seven cases early in the investigation, owing to faulty technique.

Among 176 untreated patients in whom the Weil-Felix test was carried out on two occasions at weekly intervals, 60·2 per cent. showed a rising titre; and among 118 untreated the Rickettsia-agglutination reaction showed a rising titre in similar conditions in 45·8 per cent.

In more than 20 per cent. the Widal reaction was positive at some stage. The treatment did not influence the titre of agglutination in any of the reactors. Stress is laid on the necessity for early treatment.

Intravenous injections were given in some cases, but this route was soon abandoned; it was thought probable that one or two of the deaths might have been due to these injections. *John W. D. Megaw.*

MEDICAL J. AUSTRALIA. 1944, June 24, v. 1, No. 26, 592. **Endemic Typhus.**

A statement is here reproduced from the Chairman of the National Health and Medical Research Council in which it is pointed out that 174 cases of endemic typhus were reported during 1943. Of these, 124 occurred in metropolitan areas—Sydney (11), Melbourne (1), Brisbane (11), Adelaide (1) and Perth (100). It is accepted that this disease originates in rats and is flea-borne, and the statement points out that the incidence is higher than ever before, and draws attention to the increased risk of endemic typhus and of the importation and spread of plague. *Charles Wilcocks.*

MÜHLENS. Ein Fall von Rattenfleckfieber aus dem Mittelmeerraum. [**A Case of Rat Typhus in the Mediterranean Area.**] *Deut. med. Woch.* 1943, Dec. 10, v. 69, No. 49/50, 832–3.

The author reports a case, which appears, almost certainly, to have been one of flea-borne typhus. The patient was a German soldier quartered in an isolated house near a small mountain village in Crete.

Exposure to the risk of louse-borne typhus could be excluded and rats were found on the premises.

The case would not call for comment but for the surprising fact that the chief ground on which the author excluded louse-borne typhus was a positive agglutination reaction to *Proteus X19*, 1–3,200 and to *Pr. X2*, 1–400. A table is reproduced, apparently from a recent text-book, in which the fevers of the typhus group are classified according to the types of *Proteus*-agglutination reaction; in this the flea-borne fevers are shown as giving a weak reaction with *Pr. X2*, and this organism is not shown as being agglutinated in cases of louse-borne typhus. [Apart from the inherently faulty nature of the table the author seems to have fallen into the elementary error of assuming that such tables show types of reaction which are constantly found, whereas, of course, they can only show average types and the actual findings are subject to a wide range of variation.] *John W. D. Megaw.*

PETERSON, O. L. **Therapeutic Effects of Forbisen and of Toluidine Blue on Experimental Typhus.** *Proc. Soc. Exper. Biol. & Med.* 1944, Mar., v. 55, No. 3, 155–7.

Among a large number of drugs that were tested, Forbisen and toluidine blue were the only ones giving appreciable results in the treatment of experimental typhus fever in mice.

The drugs were given mixed in various proportions with the diet ("fox chow") and the mice were inoculated intraperitoneally, before or after drug administration was started, with suspensions of yolk-sac cultures of murine Rickettsiae, in doses which killed 80 to 100 per cent. of untreated animals.

"Forbisen" was found to be moderately effective. In one test 14 of 24 mice survived when the drug was added to the diet in the proportion of 2·5 per cent. All the untreated controls died.

Toluidine blue was found very efficacious in preventing death, and the animals that died survived longer than the controls. The optimum dosage was 5 to 20 mgm. daily; this represented a concentration in the food of 0·25 to 0·75 per cent. Among 19 mice fed on a concentration of 0·5 per cent., beginning 24 hours before infection, there were 14 survivors; and among 20 others in which the drug was started at the time of infection 15 survived. In another group of 20 the drug was started 24 hours after infection and 10 survived. Only two of 20 control mice survived.

When the administration of toluidine blue was started 48 to 72 hours after infection there was no significant reduction in the mortality rate.

In similar experiments on cotton rats no benefit was observed, but these animals were inoculated intracardially with Rickettsiae, and they fed only at night and irregularly.

Toluidine blue had a marked action in reducing the toxicity and infectivity of murine Rickettsiae *in vitro* when added to suspensions of the organisms at a concentration of 1 in 10,000. The suspensions were kept nearly at the freezing point for an hour and then injected intravenously into mice. Of 18 mice inoculated with varying doses of the treated suspensions only four died, all of infection; there were no survivors among 18 mice injected with the same doses of untreated suspension and of these 11 died within two to eight hours of intoxication; the rest died later of infection. When very large doses of the treated suspensions were given all the mice died of intoxication.

When epidemic strains of Rickettsiae were treated in the way described above, there was no reduction in their toxicity, but when they were kept in contact with the drug for three hours in the cold or for one hour at 37°C., there was some reduction.

John W. D. Megaw.

YELLOW FEVER.

BATES, M. **Observations on the Distribution of Diurnal Mosquitoes in a Tropical Forest.** Reprinted from *Ecology*. 1944, Apr., v. 25, No. 2, 159–70, 1 fig. [15 refs.]

This paper deals mainly with the habits of *Haemagogus capricorni*, which is one of the chief carriers of jungle yellow fever in Colombia. This mosquito is to be found most commonly in the forest canopy and comes into contact with man, particularly when the trees are cut down. The author considers that *Haemagogus* is kept in the tree tops by a response to the humidity gradient: an avoidance of zones with a relative humidity exceeding 85 per cent. It becomes more abundant at ground level in open dry localities or after a succession of clear days. Other species of mosquitoes have not been studied in such detail, but their distribution in the forest is believed to be due to reactions to light, temperature and humidity, different species having different preferenda in the same gradients. As a result some prefer ground level, some prefer the tree tops, others have a random distribution. The diurnal mosquitoes of the forest fall into two groups: those with peaks of activity in the morning and afternoon (*e.g.*, *Psorophora ferox*) and those with a single peak towards midday (*e.g.*, *Haemagogus capricorni*). Although there are some exceptions the metallic, bright-coloured species seem to predominate at the upper forest levels, the non-metallic species at ground level. This is in accord with the view that metallic coloration is an adaptation to life in relatively dry environments.

V. B. Wigglesworth.

DE ASSUMPÇÃO, L. Provas de imunização e neutralização cruzadas entre o virus neurotrópico da febre amarela clássica e o virus isolado de doentes de febre amarela silvestre na epidemia de 1936–1937, no Estado de São Paulo. [**Cross-immunization and Neutralization between the Viruses of Yellow Fever and the Jungle Type isolated in the São Paulo Outbreak of 1936–37.**] *Arquivos de Hig. e Saúde Pública*. São Paulo. 1943, May, v. 8, No. 18, 91–108. [14 refs.] English summary.

Camondongos [a Brazilian house-rat], guineapigs and rabbits were immunized with three strains of virus: a classical neurotropic strain, F654, and two strains, D2 and D12, from two patients suffering from the jungle type of yellow fever. In a series of protocols described in the letterpress, the author shows first that the animals concerned were properly immunized. Next, that the camondongos which had been immunized with the classical yellow fever virus were immune to both the jungle strains. The corollaries of this were also proved, namely, that animals immunized by either of the jungle strains were immune to inoculation by either of the others, whereas all the controls died.

He then proceeded to make neutralization tests, by which the virus of either of the jungle types and that of the classical type were neutralized by the serum of either D2 or D12, and either of the latter viruses was neutralized by serum of the first and the serum of the other. In the words of the author :

(*a*) Serum of normal rabbits or of those inoculated with brain tissue (without virus) protected none of five camondongos infected with yellow fever virus (0/5).

(*b*) Immune serum of F654-protected camondongos inoculated with the same virus protected all (5/5), showing that in the former test death was due to yellow fever and not to some accidental contamination.

(*c*) Immune sera prepared with D2 and D12 neutralized the virus of yellow fever (F 654), all five camondongos surviving (5/5).

(*d*) Similar tests were made with sera of guineapigs immunized or vaccinated with virus F 654 and with D 12.

(*e*) The results of protection tests were the same as those made with the rabbit immune sera, confirming the previous tests of cross-neutralization between these jungle yellow fever viruses.

H. Harold Scott.

JONES, T. C. & MAURER, F. D. **Attempts to produce Jaundice in Horses by Inoculation of Yellow Fever Vaccine.** *Bull. U.S. Army Med. Dept.* 1944, May, No. 76, 115–20.

" Forty horses were inoculated with yellow fever vaccine from lots which were associated with the occurrence of jaundice in man. Ten horses received vaccine which had not been icterogenic to man. Four horses were given human plasma and serum which also may have produced jaundice in man. No disease resulted which could be compared to the human disease known variously as " catarrhal jaundice," epidemic hepatitis, infectious jaundice, and " postvaccinal hepatitis." Yellow fever virus was not detected in the serum of horses following subcutaneous inoculation of vaccine containing living virus."

DENGUE AND SANDFLY FEVER.

STEWART, F. H. **Dengue. Analysis of the Clinical Syndrome at a South Pacific Advance Base.** *U.S. Nav. Med. Bull.* 1944, June, v. 42, No. 6, 1233–40, 4 coloured figs. on 2 pls. & 1 chart.

In a South-Pacific island 25 per cent. of the military population were attacked by dengue, and 80,000 man-power days were lost.

The author describes the signs and symptoms observed in about 300 cases ; the incidence of some of these is stated to have been as follows, the figure in brackets are percentages : Sudden onset (78), frontal headache (88), chilly feeling (51), true chill (9), pain in the eyes (69), redness of the conjunctivae (94), low backache (70), pain on movement of eyes (25), palpable spleen (10), gastro-intestinal disturbances (17), " rash A " (35), " rash B " (18), " saddle temperature " (25), cervical lymph nodes (75).

" Rash A " is described as an evanescent toxic type of rash which appears on the third to the fifth day ; it is morbilliform and suggestive of rubella, or it may be a diffuse scarlet redness of the chest, shoulders

and arms. " Rash B," when it occurs, in much more characteristic ; it usually appears on the seventh day, very rarely before the fifth. It resembles a shower of petechiae, and is most abundant on the outsides of the feet, but may extend to the legs or even to the thighs. It may be preceded by distressing pruritus.

The " saddle temperature " is described as being one with high fever at both ends ; it may not touch normal between these two spells of fever. Sometimes there was a single spell of fever lasting four days. The duration of the febrile stage did not exceed seven days. An irregular spiky fever curve was sometimes seen. [The fever curve may have been modified by acetyl salicylic acid which was given as a routine to patients with severe pain.]

The cervical lymph nodes occurred as a chain of pea-sized nodules at the base of the neck over the posterior scalenus muscles.

The blood picture was of the usual type.

Treatment was purely symptomatic ; it consisted in, reassurance, rest in bed, and sedatives. Half a grain of codeine and the usual doses of acetyl salicylic acid, at bedtime, were needed in most cases.

Four good sketches in colour illustrate the paper.

John W. D. Megaw.

STEWART, M. A. **Dengue Fever.** *Proc. & Papers 13th Ann. Conference California Mosquito Control Ass., 1944, Feb. 28 & 29, Berkeley, Ca.* 5–6.

KHODUKIN, N. I., SOSHNIKOVA, M. N. & KEVORKOVA, V. I. [**On the Cultivation of the Virus of Sandfly Fever.**] *Zhurnal mikrobiologii, epidemiologii i immunibiologii.* Moscow. 1943, No. 10/11, 54–9. [In Russian.]

As some authors have suggested that only a few viruses (smallpox, the sarcoma of Rous and a few others) give characteristic changes on the chorio-allantoic membrane by the methods of Goodpasture and Maitland [*Bulletin of Hygiene,* 1935, v. 10, 563 ; 1941, v. 16, 138], the authors have decided to test the virus of sandfly fever inoculated from infected human beings. This was made possible by the wide use of an infection with sandfly fever for the treatment of some forms of schizophrenia. For the cultivation of the virus a strain from one particular patient was used. Before the experiments the strain was frequently transmitted through patients of the mental hospital, and invariably produced typical sandfly fever. All sera were subjected to a Wassermann reaction and were tested for bacterial sterility. The incubation of the serum on the chorio-allantoic membrane is described in detail. The histological changes of the membrane were as follows : usually on the 5th day after incubation 2–3 patches with a diameter of 2–3 mm. were noticed ; they were of opal white colour, their outlines were smooth and they were mostly oval in shape. They appeared not only at the site of the inoculation, but also some distance away from it. The non-specific macroscopic changes on the membrane, which are also obtained with Tyrode's solution and with normal serum, were observed by the authors, as described by others, but with some experience these changes would easily be distinguished from the patches produced by the sand-fly fever virus. Generally speaking the microscopic changes produced by the virus are thickening of the epiderm (rarely of the

entoderm) and a reaction of the mesoderm. The appearance of papillomata was attributed to the non-specific process. The formation of pearls, ulcers, etc., was due to trauma and was hardly seen when Goodpasture's technique was accurately performed. The best criterion of successful culture of the virus on the chorio-allantoic membrane is the pathogenesis of the cultures to man. Only 36·7 per cent. of inoculated eggs produced visible macroscopic changes. This indicates that the chorio-allantoic membrane is probably not the most suitable medium for the virus of the sandfly fever. *H. W. Swann.*

KHODUKIN, N. I. & SHTERNGOLD, E. J. [**Further Study of Experimental Sandfly Fever in Animals.**] *Zhurnal mikrobiologii, epidemiologii i immunibiologii.* Moscow. 1943, No. 10/11, 60–62. [In Russian.]

Having previously had successful results from infecting rabbits and dogs with the virus of sandfly fever, the authors compared two methods of infection: (1) The intracerebellar (Utenkov), and (2) The intracisternal by suboccipital puncture. Only one rabbit reacted slightly. The authors came to the conclusion that the intracerebellar method was not successful and that the virus did not survive in the brain of rabbits. The authors also tried the intracerebral method on white mice and found that these animals were not susceptible to the virus of sandfly fever. The methods were then tried on two monkeys, but the results were unconvincing and the blood of the monkeys, which was injected into five mice and two schizophrenic patients intracerebrally, gave negative results. SHORTT, POOLE and STEPHENS [this *Bulletin*, 1935, v. 32, 171] were the only workers who obtained positive results by infecting monkeys with the virus of sandfly fever. Their animals showed a definite and characteristic temperature with a definite incubation period (3–3½ days). What is more important, they were able to infect healthy monkeys and men by injecting into them the blood of the sick monkeys.

Suboccipital injection of rabbits with the virus of sandfly fever so far remains the only successful method. *H. W. Swann.*

PLAGUE.

PALESTINE: DEPT. OF HEALTH. ANN. REP. FOR YEAR 1942. 13–17, 1 map. **Plague.**

In Northern Palestine there were five cases of plague in 1942; three were infected in Haifa, where 0·3 per cent. of 9,750 rats were found to be infected. Of the rats 19 per cent. were *R. rattus*; of the fleas 80 per cent. were *Xenopsylla cheopis*. Control measures, similar to those previously reported [this *Bulletin*, 1943, v. 40, 538], are being continued, and the epizootic is apparently diminishing.

In Jaffa, in the winter of 1942–43, there were 15 cases of plague, nine of which were fatal; 88 infected rats were found in 3,860 examined. *Rattus rattus* accounted for only 1·5 per cent. of the rats; *X. cheopis* for 38 per cent. of the fleas. Rat destruction was undertaken, and 16,800 persons were inoculated with Haffkine's vaccine. Many shacks were demolished and rubbish heaps cleared. *Charles Wilcocks.*

KALLAT, S. **Recent Experiences in the Symptomatology and Treatment of Plague.** *Indian Med. Gaz.* 1944, Apr., v. 79, No. 4, 168–9.

This account relates to an outbreak of plague which involves 290 cases. One or other of the sulphonamides was used in treatment with somewhat disappointing results, for the mortality was 42 per cent. It is conjectured that this result was due to the lateness of the treatment.

W. F. Harvey.

PERYASSÚ, A. G. O combate ao rato. [**The Anti-rat Campaign.**] *Folha Med.* 1944, Mar. 5, v. 25, No. 5, 33–7.

The account here given is good, detailed, and follows the usual lines in describing how to get rid of the danger of the plague rat. A short reference is made to the history of invasion of Brazil by plague, and the bionomics of plague are considered by way of introduction. Other headings are : the damage done by rats ; species of rats ; and details of the rat destruction campaign.

Poison bait formulae are given, all of which use arsenic with a common base of wheat flour or manioc and different mixtures of flesh, fish or blood. Insistence is made on the necessity of ringing the changes on different baits, because in time rats become wary, and the baits set for them ineffective. The arsenic, preferably commercial arsenic, is present in 15 per cent. strength. Other poisons which may be used are barium carbonate and red squill. One of the advantages of the arsenic bait is that the rat, after dying, undergoes mummification.

W. F. Harvey.

BACILLARY DYSENTERY.

BULL. U.S. ARMY MED. DEPT. 1944, Apr., No. 75, 3–4. **Toxic Reactions of Sulfaguanidine Therapy.**

Sulphaguanidine was used to treat 191 ambulatory carriers of the Flexner W type of dysentery bacilli ; the dosage was 3·5 gm. three times a day for 10 days, the total amount given being 105 gm. The patients were soldiers on duty (light where possible) in a tropical island. The treatment had to be stopped in 11·5 per cent. of them owing to the occurrence of severe reactions. Fever developed in 9·4 per cent. and subsided within 24 hours after withdrawal of the drug. Intermittent crystalluria was observed in 26·5 per cent. of 83 patients whose urine was frequently examined, and transient haematuria occurred in four cases. Other reactions were urticaria (3) and scarlatiniform rash (2). About 20 per cent. of the patients complained of such symptoms as headache, backache, and nausea. The authors suggest that the loss of fluid by perspiration in the tropical climate was a contributing factor in the development of these reactions. [See also *Bulletin of War Medicine*, 1943, Mar., v. 3, No. 7, 407 ; *ibid.*, 1944, July, v. 4, No. 11, 676.]

J. F. Corson.

i. COMPTON, A. **Phage Therapy in Diarrhoea and Dysentery.** [Correspondence.] *Lancet.* 1944, Aug. 5, 192–3.

ii. BOYD, J. S. K. **Bacteriophage in Bacillary Dysentery.** [Correspondence.] *Ibid.* Oct. 7, 486.

i. Referring to an annotation in the *Lancet* of June 3rd, 1944, on a paper by BOYD and PORTNOY [this *Bulletin*, 1944, v. 41, 569], the author states that the German bacteriophage used by them for the treatment of German prisoners of war in North Africa was tested by him in 1935 and in 1942. On the first occasion he reported that the phage was ineffective against 42 per cent. of the dysentery organisms commonly met with in Alexandria, and was inferior to a phage made in Paris, tested at the same time ; in 1942 he reported that the German phage appeared to be " only moderately rich in anti-dysentery elements and almost devoid of co-dysentery activity."

He refers to Salmonella and coliform organisms as co-dysentery elements and considers that for phage treatment to be of any therapeutic value it must be effective against these organisms as well as against the classical organisms of dysentery. He therefore gives a good dysentery and meta-dysentery phage preparation alternately with a good Salmonella and coliform phage preparation [see this *Bulletin*, 1942, v. 39, 36], and thinks that if Boyd and Portnoy had treated their patients with such preparations, their results would have been different. [See also this *Bulletin*, 1943, v. 40, 845.]

ii. Boyd states that in their paper he and PORTNOY showed that the bacteriophage used by them was superior both to " Bacti-dysenteriphage " of the Laboratoire de Bacteriophage, Paris, and to " Anti-diarrhoea Polyphage " of the Bacteriophage Research Institute of Egypt. He knows of no evidence which incriminates the organisms which COMPTON has somewhat recently come to regard as important concomitants in dysentery, but agrees that a phage preparation which " covers only the classical organisms " is ineffective.

J. F. Corson.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

RATCLIFFE, H. L. & PARKINS, Phyllis V. **On the Use of Mallory's Phosphotungstic Acid Hematoxylin for staining Intestinal Protozoa.** *J. Lab. & Clin. Med.* 1944, May, v. 29, No. 5, 534–5.

The following method of staining intestinal protozoa is simpler than that of Heidenhain with iron haematoxylin, and is satisfactory for routine examinations. Fresh specimens of faeces should, of course, be used.

1. Fix smears in Schaudinn's fluid, or a modification of it containing 5 per cent. of acetic acid, for 1–24 hours ; Bouin's fluid is not suitable.

2. Remove $HgCl_2$ with iodine and the iodine with 70 per cent. alcohol in the usual way and wash in water.

3. Stain with Mallory's phosphotungstic acid haematoxylin for 20–30 minutes, the time being found by trial as it depends on the " ripeness " of the stain.

4. Wash until the smear becomes blue, dehydrate slowly in 95 per cent. alcohol and then absolute alcohol.

The protoplasm is pale blue and the nuclei a darker blue.

J. F. Corson.

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

RUIZ SÁNCHEZ, F. Fiebre recurrente en el Estado de Jalisco. [**Relapsing Fever in Jalisco State, Mexico.**] *Medicina.* Mexico. 1944, June 10, v. 24, No. 461, 199–203, 2 figs.

The author believes the case recorded here to be the first published in the State of Jalisco. The patient was a man of 23 years, in excellent health, when he was sent with others to the north-west of the State to fetch some bulls for bull-fighting. He made the journey on horseback, spending the nights at Jalostotitlán and Encarnación de Diaz, sleeping on the floor of the taverns above the stables, and was much bitten by ticks. A week later he felt ill, with intense headache, pains in the loins and calves, and nausea and vomiting; he had shivering attacks and "high fever," but did not know how high. After five days the symptoms subsided suddenly and for a week he felt well and returned to his work. Seven days later the symptoms returned, but lasted for three days only. Having passed through two more relapses, each of three days after an afebrile period of a week, he went to a doctor for treatment. No spirochaetes were seen on examination of blood-smears, but inoculation of white rats with 5 cc. of blood gave a positive finding in the rat's blood after a week's incubation. Neosalvarsan, two doses of 0·3 gm. at a three-day interval, was given; the symptoms subsided and did not recur. Ticks were obtained from Jalostotitlán and Encarnación de Diaz. They proved to be *Ornithodorus turicata*, and several of those from the latter place were found to be infective; none was found among those from Jalostotitlán. Further study is suggested to determine the extent of the district infected. *H. Harold Scott.*

EAGLE, H. & MAGNUSON, H. J. with the technical assistance of Arlyne D. MUSSELMAN. **The Therapeutic Efficacy of Penicillin in Relapsing Fever Infections in Mice and Rats.** *Pub. Health Rep.* Wash. 1944, May 5, v. 59, No. 18, 583–8.

The authors have tested the effect of penicillin on infections with a virulent strain of *Spirochaeta novyi* in both rats and mice. The results are given in tabular form and show that in white rats, to cure 50 per cent. of the animals approximately 130,000 units per kilo. body weight were required, and to cure 95 per cent. a dose of 400,000 units per kilo. The latter approached the toxic level of the commercial penicillin employed. In white mice approximately 100,000 units per kilo. were necessary to cure 50 per cent.

These results indicate that the curative dose of penicillin in man would be of the order of 25,000,000 units, and unless relapsing fever in man is more amenable to treatment than in experimental animals, the therapeutic use of the drug would not seem warranted except in arsenic-resistant cases [but see this *Bulletin*, 1944, v. 41, 293, 759.] *E. Hindle.*

WITZBERGER, C. M. & COHEN, H. G. **Rat-Bite Fever: Comparison of the Spirochetal (Sodoku) and Bacillary (Haverhill Fever) Forms.** *Arch. Pediatrics.* 1944, Mar., v. 61, No. 3, 123–33. [27 refs.]

The authors have seen seven cases of rat-bite fever in New York City during the past few years and give a discussion of the two clinical syndromes encountered, one caused by *Spirillum minus* and referred to as sodoku, and the other caused by *Streptobacillus moniliformis* and known as Haverhill fever. [See this *Bulletin*, 1942, v. 39, 693.]

Each form of rat-bite fever is separately discussed as to aetiology, clinical picture, laboratory findings, treatment, etc., and a case of each variety is described in detail. The following table gives a comparison of the two syndromes which may serve as an aid in differential diagnosis.

Comparison of the Two Syndromes as an Aid in Differential Diagnosis

	Sodoku	Haverhill Fever
(1) Causative organism	Spirochaeta morsus muris	Streptobacillus moniliformis
(2) Transmission ...	Bite of rat; occasionally other animals	Bite of rat or other animal. Possibly contaminated food
(3) Incubation period	5 to 30 days. Average 13 days	2 to 10 days. Average 5 days
(4) Wound from bite	Apparent healing followed by chancre-like ulceration	Heals promptly without subsequent induration or exacerbation
(5) Lymph glands ...	Regional lymphadenitis	Not involved
(6) Systemic manifestations	(*a*) Regularly relapsing type of fever (*b*) Generalized maculopapular rash (*c*) Varying degrees of prostration and debility (*d*) Arthritis very rare	(*a*) Intermittent but not regularly relapsing type of fever (*b*) Macular and petechial eruption (*c*) Varying degrees of prostration (*d*) Metastatic arthritis is common
(7) Laboratory findings	(*a*) Polymorphonuclear leucocytosis (*b*) Secondary anaemia (*c*) Kahn tests usually positive (*d*) Isolation of spirochaete by animal inoculation of blood or infected lymph gland material (*e*) Agglutination tests negative	(*a*) Same (*b*) Same (*c*) Negative (*d*) Isolation of Streptobacilli moniliformis by blood culture on veal infusion broth enriched with rabbit serum (*e*) Agglutination tests with Streptobacillus positive. Serum from patients agglutinates a polyvalent antigen of the organism
(8) Treatment ...	Responds to treatment with arsenicals	Arsenicals of little or no value. Sulphonamides may be indicated

E. Hindle.

HITZIG, W. M. & LIEBESMAN, Ada. **Subacute Endocarditis associated with Infection with a Spirillum. Report of a Case, with Repeated Isolation of the Organism from the Blood.** *Arch. Intern. Med.* 1944, May, v. 73, No. 5, 415–24, 3 figs. [Refs. in footnotes.]

A detailed account of a fatal case of subacute endocarditis associated with infection with *Spirillum minus*, which was isolated from the blood

on six occasions, extending over nearly 10 weeks, and cultured in dextrose and tomato bouillon in an atmosphere containing 3·5 per cent. CO_2. The nature of the organism was established by its morphology, and also by its pathological and serological characters. Reference is made to a spirillum, *S. surati*, isolated from the blood of a case of subacute endocarditis by LAMB and PATON [*Arch. Int. Med.*, 1913, v. 12, 259] but its cultural and serological reactions are shown to be quite distinct from those of the organism isolated by the authors.

The main interest of this case lies in the close resemblance of the clinical course and changes observed at autopsy to those observed in cases of the common form of subacute bacterial endocarditis due to *Streptococcus viridans*. *E. Hindle.*

CONGE, M. & BOYER, F. Chimiothérapie du sodoku expérimental du cobaye par le sulfamide et ses dérivés. [**The Chemotherapy of Experimental Sodoku in the Guineapig by Sulphonamide and its Derivatives.**] *Ann. Inst. Pasteur.* 1944, Mar.-Apr., v. 70, No. 3–4, 119–24, 2 figs.

The authors mention that in a previous communication with NITTI [reference not given], they had shown that it was possible to treat guineapigs infected with sodoku by means of subcutaneous implantation of fragments of sulphanilamide. The dose was 1 to 2 gm. per kilo. body-weight administered two or three times at intervals of 6 or 8 days. The authors now find that it is much more satisfactory to give the drug by mouth, as with the first method certain animals died under the treatment.

It is noted that in testing the effect of treatment it is preferable to use a virulent strain of the spirillum, inoculated intradermally, and adult guineapigs, which give a better symptomatology. Under these circumstances a chancre appears at the site of the inoculation, after an incubation period of three to four days, which reaches its maximum development at the end of the week. During the next week spirilla appear in the blood but show marked daily variations in the numbers present. From the beginning of the third week various trophic disturbances appear and the animal dies between the 30th and 40th days of the disease.

Treatment by means of 1162F. [sulphanilamide] administered daily by mouth in doses of 0·5 gm. per kilo. body weight was found to cure every animal treated, even if the treatment was not begun until late in the infection—towards the 30th day. The spirilla disappeared from the blood within five or six days and the general symptoms subsided. The treatment was also successful in the case of animals *in extremis*.

When the dose was reduced to 0·1–0·2 gm. per kilo. body-weight, treatment was successful in preventing infection if it was begun on the same day as the inoculation of the spirilla, but did not cure animals in which the disease had developed. Attempts were then made with allied compounds which are eliminated more slowly from the body, and it was found that daily doses of 0·1 gm. sulphathiazole, or of sulphapyridine, for 12 days, cured animals up to the 20th day of the disease.

The treatment, in nearly every case, was accompanied by a sharp rise in the number of spirilla in the blood about the second day, lasting for 24 to 48 hours, after which the number rapidly diminished. In some

cases there was a secondary rise two or three days later. The body-weight of the guineapigs showed a constant diminution during the first few days of treatment, followed by a steady increase after about a week. *E. Hindle.*

HELMINTHIASIS.

OTTOLINA, C. & ATENCIO M., H. Nuevos caminos para el diagnostico clinico preciso de la schistosomiasis Mansoni. [**New Methods for the Exact Clinical Diagnosis of Schistosomiasis caused by** *Schistosoma mansoni.*] *Rev. Policlinica Caracas.* 1943, Nov.-Dec., v. 12, No. 73, 348–80, 2 figs. [18 refs.]

The authors discuss the reason why they are not satisfied with current methods of diagnosis of this disease. They review the work of earlier authors on its incidence in Venezuela and Egypt and conclude that the methods used in Venezuela fail to diagnose clinically 11 to 18 out of every 20 cases. This failure is the more serious because the methods used are employed by experts, whose figures of the incidence presumably represent the highest percentages obtainable by these methods. After a discussion of the limitations of the complement-fixation reaction, the authors discuss the use of biopsies of liver parenchyma and of tissue taken from the rectal ampulla.

Biopsy of the liver was tried after examination of bile removed by duodenal incubation of 33 patients, in whose faeces eggs of *S. mansoni* had been found, had revealed these eggs in two only. The authors concluded that the examination of extrahepatic bile was useless for diagnosis. A technique was then developed at autopsies for removal of small samples of liver tissue and their "digestion" by Fergusson's method (*Glasgow Medical J.*, 1935, v. 79, 14–23) in 4 per cent. KOH at 60–80°C. The final procedure adopted by the present authors was to put three drops of 4 per cent. KOH into a centrifuge tube and to add to this the piece of liver tissue removed by means of a trochar and syringe. This fluid was then warmed on a spirit lamp and after 3–5 minutes the liver fragment was "digested." The digest can then be centrifuged and the deposit examined for eggs of *S. mansoni*. The pieces of liver can also be examined by teasing up in saline or by clearing in lactophenol. Out of 40 livers examined thus by "digestion" at autopsy, 18 (45 per cent.) contained the eggs. Relating this figure to published figures of the incidence, the authors conclude that 25 out of each 45 cases are not diagnosed at autopsy by current methods.

This procedure was then tried on living patients in whose faeces eggs of *S. mansoni* had been found. Out of 16 such patients liver material could only be obtained from 9, but all these contained eggs of *S. mansoni*. There was, however, a serious risk of haemorrhage, although the authors did not experience this in any of their cases. They therefore sought another method and tried biopsy of the rectum.

The method was first tested at autopsies. Pieces of the rectal ampulla put into 10–15 cc. of KOH at 60–80°C. were "digested" in ½–1 hour. Of 25 such specimens eggs were found in 15 (60 per cent.), often in extraordinary numbers. The results showed that the rectum contained eggs more often than the liver, and that they were never absent from the rectum when they were present in the liver. The bearing of these

results on views about the incidence of infestations which have become inactive is discussed. The view of the authors is that the rectum and sigmoid are more often infested than the liver.

On living patients the authors performed rectoscopy and biopsy of a fragment of the free border of the right dorso-ventral valvular fold (coccygeal-sacral fold) of the upper half of the rectal ampulla. Their technique is described. A piece of tissue the size of a grain of rice was removed and " digested " in KOH. For these examinations sanatorium patients were used, whose better social status had exposed them less to infestation ; some came from regions where bilharziasis is not recorded. Previous faecal examination of 192 of them had revealed eggs in the faeces of 19 (9·89 per cent.). Rectal biopsy was done on 12 of these positive cases. No treatment had been given to 8 and the biopsies on all of these were positive. One had been treated, but was still positive by faecal examination and the biopsy was also positive. Two were regarded as clinically cured on the basis of successive faecal examinations after one or two courses of tartar emetic, but the biopsies on both were positive. One biopsy only was negative and this was in a clinically cured patient who had had three courses of fouadin. It was thus evident that one or two courses of treatment with tartar emetic controlled by routine faecal examinations were not sufficient evidence of a cure. Biopsy, moreover, took only a few hours, while faecal examinations might have to extend over several months.

Biopsy of the rectal ampulla was also done on 100 sanatorium patients whose faecal examinations were negative. Biopsy of 11 of these (11 per cent.) revealed the presence of eggs of *S. mansoni*. Multiple or successive biopsies of different parts of the upper half of the rectal ampulla would, the authors suggest, increase the incidence figures still more. Biopsy could supplement skin and complement fixation tests. The paper itself must be consulted for the authors' discussion of incidence figures obtained at autopsy or otherwise and their relation to their own findings by liver or rectal biopsy.

G. Lapage.

Di Prisco, J. Nota preliminar sobre posibles dermatosis de origen bilharziano y su diagnostico por la prueba cutanea de la bilharzina. [**Preliminary Note on possible Dermatoses of Bilharzial Origin and their Diagnosis by a Cutaneous Test with Bilharzial Antigen.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1943, Oct., v. 8, No. 5, 1067–72.

The author deals with certain cutaneous syndromes, distinct from cercarial dermatitis or the nodular erythemas which have been ascribed to bilharzial infestation. These are described as :—

1. *Neurodermatitis*, which is the most frequent. The patient shows one or more plaques of lichenification, sometimes circumscribed by a well-defined border, sometimes diffuse, or occasionally generalized. These plaques are very pruriginous. Their surface is glossy, hyperpigmented and divided into squares by the crossing of numerous sulci ; the condition may resemble lichen planus. The plaques are chiefly found on the dorsum of the foot, in the popliteal space, on the flexor surface of the elbow, or at the nape of the neck. Biopsy has shown, in some cases, a rich eosinophile infiltration.

2. A type called *chronic prurigo*, characterized by a papular eruption which occurs especially on the extensor surfaces of the limbs and is very pruriginous. The eruption usually occurs on a thickened skin.

3. A non-purulent pruritus without any discoverable cause (*i.e.* without diabetes, gout, hypocalcaemia, endocrine factors, alimentary or respiratory allergy, neuroses, etc.). But the bilharzial reaction is positive in these, and sometimes eggs of *Schistosoma* are found in the faeces.

Dr. P. GUERRA suspected that all these might be bilharzial, and the author discusses this view. It is necessary, he says, not to draw hasty conclusions from the insufficient facts available and he comes to no conclusion himself, but he gives the following observations :—

Intradermal tests were done, after consultation with Prof. M. MAYER, with antigen prepared by Mayer's technique from adult *Schistosoma*. It was recognized that allergic reactions due to factors other than the presence of *Schistosoma* might be obtained. These intradermal tests were done on 112 patients, who were not selected. Of these 53 (47·3 per cent.) were positive and 59 (52·6 per cent.) were negative. Of the 59 negatives, 7 only had been diagnosed as prurigo or lichenification, the rest having asthma, urticaria, etc. Of the 53 positives, 27 (50·9 per cent.) had been diagnosed as prurigo or lichenification. None of the 59 patients negative to the intradermal tests had eggs of *S. mansoni* in the faeces ; but these eggs were found in the faeces of 16 out of 39 of the patients giving a positive intradermal test (the faeces of 14 of these could not be examined). The Fairley complement fixation test was done on three of the patients positive to the intradermal test and it was positive in all three. In an attempt to differentiate between bilharzial and other allergic reactions, the patients positive to the intradermal test were divided into group A, who were not positive to any other allergic test (alimentary or respiratory allergies) tried, and group B who were. Antibilharzial treatment given to group A improved many and cured a few, but the same treatment given to group B gave inconclusive results. Asthmatic patients were seen in whom the only positive skin test was the one done with bilharzial antigen ; anti-bilharzial treatment improved these. *G. Lapage.*

CAWSTON, F. G. **Propamidine in Bilharziasis.** *South African Med. J.* 1944, July 8, v. 18, No. 13, 228–9.

Propamidine was tried in a few cases of urinary schistosomiasis in South Africa. Courses of injections, i.m. or i.v., with a total dosage varying from 0·6 gm. (children) to 1·7 gm. were given during periods of 11 to 30 days. Intramuscular injections produced induration of the arm muscles and results could not be judged in some of the cases. In two Indian youths, who received a total dosage of 1 gm. in about 10 intravenous injections during 30 days, living ova were still present in the urine at the end of the course. The injections caused syncope. In an African patient the urine became free from ova and red blood corpuscles after 11 intravenous injections of 0·15 gm. The author remarks that the drug is much more useful in staphylococcal infections of the skin and nasal cavity. *J. F. Corson.*

MACFARLANE, W. V. **Schistosome Dermatitis in the Southern Lakes. An Investigation of Swimmers' Itch.** *New Zealand Med. J.* 1944, June, v. 43, No. 235, 136–40, 5 figs. [11 refs.]

Swimmers' itch has long been known to follow bathing in certain New Zealand lakes, as in many other countries. That due to bathing

in Lake Wanaka was investigated and three types of lesions were observed and were reproduced in experiments on volunteers. In persons who had not had previous attacks, itching began from 10 to 15 minutes after leaving the water ; in some persons macules, 2 mm. in diameter, appeared after 1 hour and disappeared in six hours, but in others there was no visible lesion. In persons who had been attacked before, itching and macules also appeared, but the macules became papules in 10 hours and some develped into red weals. The third type of lesion—itching, macules and pruritic oedema—appeared in one person. In experiments on volunteers it appeared that in persons not previously attacked only macules developed, while papules were formed in those previously attacked. Some evidence of immunity was obtained ; it was local in areas of thick skin, and a general immunity was shown by some persons who had never been infested.

The life-history of the parasite is similar to that of *Schistosoma*. At Lake Wanaka three snail hosts were found—*Myxas ampulla*, *M. arguta*, and *Limnaea alfredi* : they vary in length up to 0·8 cm. and have large fleshy feet and friable shells [a photograph shows dextral helices]. The vertebrate hosts are probably ducks.

The cercaria is fork-tailed and has the following dimensions of length : body, 300–344μ ; tail 446–522μ ; tail-forks, 244–262μ. There are 5 pairs of posterior enzyme-secreting glands, used for lysis of the epidermis of the vertebrate host, and 1 pair of anterior glands, used for escape from the snail. The cercaria has a ventral sucker, a primitive nerve-mass and a pair of eye-spots, a set of flame-cells, an excretory vesicle and ducts discharging at the tips of the tail. It is closely related to *C. ocellata* and *C. elvae*, but appears to be a new species and is named *C. longicauda*.

In an experiment on a volunteer it was observed that the body of the cercaria penetrated the skin in about 5 minutes, the tail being broken off outside by a convulsive movement. The itching begins as the cercaria "digests a track through the malpighian layer." Biopsy after 24 hours showed the parasite in a burrow in the epidermis ; the prickle cells were lysed and compressed and the parasites were beginning to undergo lysis. In the dermis there were oedema and polymorphonuclear and lymphocytic infiltration. After 75 hours there was no trace of cercariae. The burrows do not pass into the dermis. No eosinophil leucocytes were seen.

Cercarial antigen was prepared from the bodies of cercariae preserved in merthiolate, and 0·1 cc. was injected intradermally into 11 infested and 10 uninfested persons. The latter did not react, but the former showed a slight immediate and a much more marked delayed reaction ; this appeared as an itching erythematous area, 1 cm. in diameter 8 hours after the injection, and consisted of a central red spot surrounded by a pink tender areola and a peripheral zone of vasoconstriction. In recently infested subjects it was 3 cm. in diameter and lasted 7 days ; in a person infested 5 years before, it was 1 cm. in diameter and lasted for 2 days only, while no reaction occurred in a person infested 10 years previously. Heterologous antigen, prepared from *Gorgodera* sp. adults, caused a similar but smaller reaction in infested, but not in uninfested, subjects. The papules are probably an allergic reaction, and the weals further responses to protein or polysaccharide liberated from the cercaria.

The snails live chiefly in the beds of pond-weed (*Myrcophylla* sp.) in less than 10 feet of water. Until the snails can be eradicated,

possibly with copper salts, people should avoid bathing there. [Other cercariae incriminated and references in this *Bulletin* are: *C. elvae*, v. 25, 946, v. 27, 459, v. 38, 378 and 379; *C. ocellata*, v. 27, 960, v. 29, 48; *C. pathlocopticum*, v. 21, 206, v. 39, 769; *C. physellae*, v. 38, 44 and 379; *C. spindale*, v. 36, 40; *C. stagnicolae*, v. 38, 44, 378 and 379; *C. vitrina*, v. 27, 960; *C. tuckerensis*, v. 34, 392; cercaria of *S. haematobium*, v. 34, 392; *C. douthitti* see PRICE, *Amer. J. Hyg.*, 1931, v. 13, 685.] *J. F. Corson.*

ARCHIVOS INTERNACIONALES DE LA HIDATIDOSIS. Montevideo. [**International Archives of Hydatid Disease.**] 1941, Dec., v. 5, No. 1–2, 680 pp., Numerous illustrations.

This volume contains a paper on the intradermal test in hydatid disease, by CASONI, one on the incidence of the disease in the United States and Canada by MAGATH [see also this *Bulletin*, 1937, v. 34, 401] who states that between 1808 and 1938 there have been records of only 501 cases in the two countries. In another paper PINTO and LINS DE ALMEIDA report on the incidence in Brazil. Most of the contributions deal with clinical aspects of the disease, but there is a considerable section of 7 papers in which biological problems are considered.

Charles Wilcocks.

RIVAS, C. I. Hidatidosis y tuberculosis pulmonar. [**Hydatid Disease and Pulmonary Tuberculosis.**] *Rev. Asoc. Med. Argentina.* 1944, May 30, v. 58, No. 534, 331–6, 17 figs.

BAILEY, W. C. **A Study of the Incidence and Treatment of Intestinal Parasites in South-eastern Kentucky.** *Southern Med. J.* 1944, July, v. 37, No. 7, 407–9.

The commonest worm in children was *Ascaris lumbricoides*, in adults *Trichuris trichiura* and *Necator americanus*.

MACGREGOR, G. A. **Sternal Puncture in Hypochromic Anaemia resulting from Ankylostomiasis.** *East African Med. J.* 1944, May, v. 21, No. 5, 134–43.

The sternal puncture and peripheral blood findings of 16 cases of severe anaemia associated with ankylostomiasis are discussed. The author describes the anaemia as hypochromic but in many cases the colour index was above 0·8, which is unlike classical hypochromic anaemia. Unfortunately no measurements of cell size were made. He describes the marrow picture as showing a definite percentage increase in the incidence of both early and late erythroblasts and a definite swing to the left in the process of maturation of the erythrocyte, again a finding which is unlike that of the hypochromic anaemias studied in other countries. Both the peripheral blood and marrow picture suggest that there is probably a dual deficiency present, namely of iron and possibly of the anti-pernicious anaemia factor. Analysis of the diet of the patients studied showed it to be extremely poor in iron, in protein and in any source of the anti-pernicious anaemia factor. The remarkable improvement seen in patients when massive iron therapy was augmented by intramuscular liver extracts tends to support this hypothesis. [Though the observations described are incomplete in certain respects, this paper is valuable because it emphasizes the extreme importance of anaemia, due to a combination of ankylostomiasis and dietary

deficiencies, in African natives. Anaemia of such severity must inevitably reduce their capacity for work almost to zero. The observations tend to support the findings of NAPIER *et al.* (this *Bulletin*, 1942, v. 39, 100) and ANDREWS (*ibid.*, 772), that hookworm infection does not produce severe anaemia unless there is also a dietary deficiency.] *Janet Vaughan.*

LOWE, T. E. & LANCASTER, H. O. **Hookworm Infestation.** *Med. J. Australia.* 1944, Apr. 1, v. 1, No. 14, 289–92.

The authors studied 386 soldiers who had returned from service in the islands north of Australia with mild infestations with *Ancylostoma duodenale*, *A. braziliense* and *Necator americanus*. Most of them also had malaria. Reliable information about skin lesions such as "ground-itch" or "creeping eruption" could not be obtained, because most of the patients had skin lesions due to fungi and other agents. One-third of the patients had flatulent dyspepsia, but similar symptoms were found in other patients in whom evidence of helminth infestation could not be found. The haemoglobin was estimated and the number of red blood cells counted in 200 consecutive patients on the third day after treatment for malaria, and these data were compared with others obtained from 100 patients with malaria but without evidence of helminth infestations. The authors conclude that the malaria and not the hookworms caused the fall in haemoglobin found (the average haemoglobin level was 85 per cent.). The only blood change due to the hookworms was, they think, the pronounced absolute eosinophilia. The maximum number of eosinophils recorded was 12,500 per cmm. and the maximum percentage 80 per cent. Averages were 1,800 eosinophils per cmm. and 14 per cent. The authors think that the absolute counts are alone useful for diagnosis. The number of eosinophils fell rapidly 24–36 hours before a malarial rigor and did not again reach their maximum until 14 days after it. The Willis concentration technique was used for diagnosis and usually only one specimen of faeces was taken from each patient, so that the authors think that they may have missed many cases. In differential diagnosis, the eosinophilia is the main problem. Of the patients with recurring malaria, 11 per cent. had an eosinophilia of 500–1,350 cells per cmm. Of all the subjects with more than 500 eosinophils per cmm. 144 had no evidence after two faecal examinations of helminth infestations. Thirty-nine showed helminth infestation after repeated examinations, in 19 the eosinophilia disappeared after anthelmintic treatment, in 61 it was adjudged to be due to the malaria, and in 25 it was an unexplained eosinophilia of 2,000 or more per cmm., without evidence of the presence of protozoa or helminths, although all these patients had recurring malaria.

For treatment the authors used hexylresorcinol (15 grains), carbon tetrachloride (3 cc.), oil of chenopodium (2 cc.), tetrachlorethylene (4 cc.), and mixtures of oil of chenopodium (1 cc.) with either carbon tetrachloride (3 cc.) or tetrachlorethylene (4 cc.). The most effective drug used alone was tetrachlorethylene but the mixtures of this with oil of chenopodium and of chenopodium with carbon tetrachloride were equally effective. The stools of 60 per cent. of the subjects were free of eggs five to seven days after a single dose of [unspecified] anthelmintic and repeated doses freed the stools in 80 per cent. of cases. But eggs were found three weeks after dosing in some cases and the authors give as a criterion of cure the absence of eggs after three examinations

at intervals of one week. The total number of doses of carbon tetrachloride given was 317. In two patients there was mild jaundice and in two others, upper abdominal pain on the right side and tenderness over the liver without jaundice. Tetrachlorethylene consistently caused pronounced muscular incoordination. The authors conclude that these symptoms show that the doses they gave were the maximum ones that can be given with safety. *G. Lapage.*

MAPLESTONE, P. A. **Hookworm Infestation.** [Correspondence.] *Med. J. Australia.* 1944, Apr. 22, v. 1, No. 17, 379–80.

The writer of this letter points out that the relative values of hexylresorcinol, oil of chenopodium, carbon tetrachloride and tetrachloride and tetrachlorethylene have been established for many years, as the result of the work of numerous investigators whose conclusions are based on many thousands of treatments, and that LANCASTER and LOWE [above] do not refer to any of this work. He thinks there is a danger that the brief statement by these authors on the toxic effects of the drugs which they used may be taken as a full statement of the position. Lancaster and Lowe do not comment on the evidence which they found in four of their patients of liver damage (jaundice and pain and tenderness in the hepatic region), and do not describe any treatment of these symptoms; nor do they seem to be aware of their grave import, they merely conclude, on their evidence, that the 3 cc. of carbon tetrachloride given by them is the maximum safe dose. Maplestone emphasizes that carbon tetrachloride is a dangerous drug, and that its toxicity is largely independent of the size of the dose; there is a record of death after only 1·5 cc. All the evidence goes to show that it invariably causes liver damage, whether there is clinical evidence of this or not. It has been superseded by tetrachlorethylene, which has approximately the same anthelmintic value against hookworms, but does not cause liver damage. No deaths have yet been ascribed to tetrachlorethylene, though there is at least one record of deep narcosis, resembling chloroform anaesthesia and lasting two hours or longer, so that it is necessary to keep patients who are given tetrachlorethylene under observation for some hours. [Most recent editions of text-books on pharmacology and tropical medicine point out the contraindications to giving carbon tetrachloride, and discuss the possibility of individual idiosyncrasy to it, and the precautions which must be taken in its use.] *G. Lapage.*

LOWE, T. E. & LANCASTER, H. O. **Strongyloidiasis in Man: Infestation with *Strongyloides stercoralis* (Bavay, 1876).** *Med. J. Australia.* 1944, May 13, v. 1, No. 20, 429–35. [13 refs.]

In the Australian area, strongyloidiasis is reported from New Caledonia, the New Hebrides, New Guinea and the East Indies generally and from the coastal belt of Queensland. HEYDON and GREEN (*Med. J. Australia*, 1931, v. 1, 619) found an incidence of 0·03 per cent. among whites on the Atherton Tableland, and think the few earlier surveys made in Australia were inaccurate because of contamination of faeces with coprophile nematodes. Two records are quoted of the incidence of strongyloidiasis outside the tropical zone of Australia. It is likely that Australian troops will be infested, and that the disease will become of clinical importance. The life history of

Strongyloides stercoralis and the pathological changes caused by the larvae and adults are described. Several fatal cases have been reported by FAUST and DE GROAT [this *Bulletin*, 1941, v. 38, 118] and by OPHÜLS [*ibid.*, 1930, v. 27, 979]. Lowe and Lancaster studied 16 cases in a military hospital; of these, 14 had served in New Guinea, 2 had never left the Australian mainland. Thirteen of them also had malaria, hookworm or other nematode infestations and other ailments, but when these conditions had responded to treatment, the effects of *Strongyloides* could be observed. The patients had been in the tropics for only a few months, so that the disease was in its early stages in all. The symptoms were chronic cough (due to larvae in the lungs), dyspepsia, and chronic diarrhoea (due to adult parasites burrowing into the intestinal submucosa). There was no anaemia. The only leucocyte change was eosinophilia. The leucocytes ranged from 8,000 to 30,000 per cmm.; the number of eosinophils from 1,100 to 12,600 per cmm. with an average maximum of 4,300 per cmm. In the eight cases without other helminths, the range was from 1,100 to 5,300 with an average of 2,570. One patient had a persistent eosinophilia of 800 cells per cmm. which increased after ten days to 5,300 per cmm., and, eight days later larvae of *Strongyloides* were found in the faeces. The eosinophilia is not diagnostic. The adult worms or their larvae must be found in the faeces. Larvae may be found by culture of 1 oz. of faeces mixed with 1 oz. of boiled garden soil in a jar in a warm dark place. After seven days, the mouth of the jar is covered with gauze and inverted into a Baermann apparatus. The larvae may be seen with the naked eye, migrating from the culture into the warm water in the Baermann funnel, or may be drawn off after one hour from the rubber tube below. The rhabditoid larvae of *Strongyloides* must be distinguished in such cultures from the rhabditoid larvae of hookworms and the pseudorhabditoid larvae of *Trichostrongylus*.

Gentian violet gave disappointing results for treatment, although it usually relieved the symptoms. Only one patient showed return of the eosinophil count to normal, and the three successive negative faecal examinations which were taken as the criterion of cure. One patient showed the three successive negative cultures, but had 7,040 eosinophils per cmm. at the end of treatment. Fouadin, tartar emetic and emetine hydrochloride all failed to affect the stages of the worms in the tissues. Problems of hygiene are similar to whose which apply to hookworm. [*Cf.* LEVIN, this *Bulletin*, 1944, v. 41, 411, and SHIKHOBALOVA and SEMENOVA [*ibid.*] who obtained similar results with gentian violet and suggest, as these authors also do, that a more serious study of strongyloidiasis is required. *G. Lapage.*

BRUNNER, M., ALTMAN, I. & BOWMAN, Katherine. **Canine Sensitivity to Ascaris Antigen.** *J. Allergy.* 1944, Jan., v. 15, No. 1, 2–8.

In a paper on spontaneous allergy in lower animals WITTICH (*J. Allergy*, 1941, v. 12, 247) reported the case of a dog showing typical symptoms of ragweed hay fever. Cutaneous tests with ragweed antigen were positive and were followed by a systemic reaction and shock, from which the dog recovered after an injection of adrenalin. Wittich suggested the possibility of spontaneous development of atopy in the dog. BRUNNER (*J. Allergy*, 1934, v. 5, 257) has shown that *Ascaris* antigen can produce reagins in man. In the present paper the

authors investigate whether *Ascaris* would produce, in dogs, skin-sensitizing antibodies with characteristics similar to the atopic reagins which *Ascaris* antigen produced in man. [Throughout the paper the generic and specific names of the Ascaroidea referred to are not stated.]

Intracutaneous tests (on the abdomen) were first done on 24 dogs aged 2 months with dog and pig *Ascaris* antigens. The cutaneous reactions were negative to both antigens in two of these dogs, aged 2 to 7 months; in two others, aged 3 and 4 months, the reactions with dog *Ascaris* antigen were negative, while those with pig *Ascaris* antigen were positive (one plus). In 10 of the 24 dogs there were positive reactions to both antigens. Hookworms, *Ascaris* and whipworms were recovered from six of the dogs which gave positive reactions to both antigens. No nematode infestation was found in four others positive to both antigens, but it was known that these four had been treated for a previous nematode infestation. Precipitin tests on six dogs, all harbouring nematodes and giving positive cutaneous reactions to both antigens, were all negative.

Constitutional reactions (tiredness, followed by panting, vomiting, rapid pulse and marked weakness) followed the skin tests on two dogs positive to both antigens and known to have had previous nematode infestation. One recovered without treatment and the other after the injection of 0·5 cc. of 1 : 1,000 adrenalin. Precipitin tests with the sera of these two dogs were negative. With the blood of one of them attempts were made to transfer the skin sensitivity to other dogs and to human beings by the Prausnitz-Küstner technique. This transfer was successful in four out of five dogs and in all the four human beings. The same transfer made with the blood of the other of these two dogs, was successful in two other human beings. Further tests with the blood of this animal were not possible.

The skin-sensitizing antibodies in the serum of a dog naturally sensitive to *Ascaris* were heat labile and resembled in this respect human atopic reagins. *Ascaris* antigen produces skin-sensitizing antibodies in human beings and the authors actively sensitized two dogs four months old with *Ascaris* extracts. Passive transfer tests with the serum of one of these dogs were negative; but they were weakly positive with the serum of the other. *G. Lapage.*

ROY. NAV. MED. BULL. 1944, No. 11, 9–11. **Filariasis.**

Some apprehension has been caused among American naval personnel stationed in the Samoan Islands by the occurrence of a number of cases of filariasis among them. The clinical diagnosis was confirmed by the discovery of adult filariae in excised tissue although in no case have microfilariae been found in the blood. A survey showed that troops were being infected in the islands Tutuila, Upolu, Wallis, Funafuti, Borabora and occasionally in the Tonga Islands. *Aëdes scutellaris* var. *pseudoscutellaris* [*Aëdes variegatus*] is the chief, if not the only, vector; dissection showed that a high percentage of these mosquitoes in the villages were infected, but very few of those caught 100 or more yards away from the villages. The disease exists in natives throughout both the Central and South Pacific areas, but it has only been found in the troops in the Central Pacific area, probably because closer association with natives has been necessary there. A different mosquito, *Anopheles punctulatus* var. *moluccensis* is the vector in the South Pacific area

[this term appears to include the New Hebrides and the Solomon Islands]. Patients should be assured that the risk of functional impairment of the reproductive organs and of the development of elephantiasis is very slight, and that spontaneous recovery is to be expected after leaving the infected area. [See also this *Bulletin*, 1944, v. 41, 599 and 860.] *J. F. Corson.*

NEUMANN, H. **Filariasis in the White Man.** *J. Trop. Med. & Hyg.* 1944, June-July, v. 47, No. 3, 25–8.

In the Samoan Islands, a newcomer of white race may show no symptoms of filariasis even when heavily infected; when symptoms are present in early filariasis they may be classified into three types:—(1) allergic; (2) due to streptococcal superinfection; and (3) due to staphylococcal superinfection. In the allergic type a diffuse oedematous swelling develops, usually in a limb but sometimes in the scrotum; there is no reddening of the skin, no pain and little or no malaise or rise of temperature. It lasts for about a week and then subsides. It is thought to be due to reaction to dead filarial worms in the tissues. It is not seen earlier than five months after arrival in the endemic area. The attacks may be repeated but the prognosis remains good and no treatment is required. When streptococcal infection, *via* the bloodstream, is superadded, lymphadenitis, followed by lymphangitis, develops; the skin shows red streaks, and fever (slight or high), malaise, tenderness and swelling of lymph glands are also present. The attack lasts for about a week or more. It usually affects the limbs or scrotum, sometimes the breasts, ears or labia. These attacks are called "mumu" in the Samoan language, the word meaning red. If they are frequently repeated during several years, elephantiasis may develop and this should be avoided by departure from the endemic area. This type can be cured with sulphonamides. The third type, due to superinfection with staphylococci, is less common in white people than in the natives; fever, local swelling and pain may occur and an abscess may form. The limbs and scrotum are the parts most commonly affected. The condition is not responsive to sulphonamides but if spontaneous absorption is slow an incision will quickly cure it. Repeated attacks do not lead to elephantiasis.

Elephantiasis and other forms of chronic lymph stasis occur after long residence; after departure from the endemic area no further increase in the condition need be expected.

Microfilariae are usually not found in the blood before the 7th year after infection as they are too few to be seen in the 20 cmm. of blood usually examined; they are sometimes found in hydrocele fluid in the second year after infection. The combined span of life of an adult worm and its microfilariae is probably about 15 years.

The diagnosis of early filariasis must rest on clinical symptoms; skin tests have hitherto been found to be unreliable. Practically the only way to prevent infection is by protective measures against mosquitoes; the vector, *Aëdes variegatus* [*Aëdes scutellaris pseudoscutellaris* of some authors] has not a long range of flight. Since microfilariae are absent from the peripheral blood, there is practically no danger that a returned patient will introduce the disease into temperate climates. Usually, after leaving the area, no further attacks occur. Except when the genital region is attacked the first

and third types of symptoms do not require the patient to leave the area. [See also this *Bulletin*, 1944, v. 41, 599, 600 and 860.]

J. F. Corson.

HARTZ, P. H. **Contribution to the Histopathology of Filariasis.** *Amer. J. Clin. Path.* 1944, Jan., v. 14, No. 1, 34–43, 9 figs.

In lesions caused by *Wuchereria bancrofti* the author found epithelioid-cell granulomatous lymphangitis in 5 out of 10 cases. In several cases which showed this histological picture, the examination of more sections led to "the finding of the filaria." Details of three cases are given. The granulomata can be found in the lumen and wall of the lymphatic vessels, in the lymph nodes and in the connective tissue. They are most typical in the lymphatics. Different aspects of epithelioid-cell granulomatous lymphangitis are found according to the age of the lesions. The simplest form is a more or less loose collection of epithelioid cells, histiocytes and lymphocytes, usually not connected with the wall of the lymphatic vessel, whose endothelium is intact; and there is no regular arrangement of the cell types. Cells transitional between histiocytes and epithelioid cells are easily found. The form of the epithelioid cells is not different from that found in tuberculous lesions; their nuclei are oval or more elongated, and often band-like or slightly curved. In a more advanced stage of the lesions the epithelioid cells are closer together with only a few lymphocytes and bands of fibrin threads between them. Lymphocytes may occur around the accumulations of epithelioid cells. There is no necrosis when the microfilariae are intact. Smaller lymphatics become occluded by this granulomatous mass, connective tissue fibres appear between the cells, and this, the author thinks, leads to fibrosis. The endothelium of the vessel is intact until it is obliterated. In the larger lymphatics the accumulations of cells are often near to or in contact with the valves, which may be thickened by cellular infiltration. This process is combined with narrowing and obliteration of the lymphatics by granulomatous perilymphangitis, the product of which resembles small epithelioid-cell tubercles with or without giant cells. It leads to narrowing of the lymph vessels whose endothelium is pushed inwards towards the lumen. It is, the author thinks, typical of filariasis that isolated granulomatous masses connected with the wall of the lymphatic, but covered with endothelium, may occur in the lumen. In the sinuses of the lymph nodes there are small groups of epithelioid cells sometimes combined with Langhans giant cells or with more atypical giant cells. There may be pronounced dilatation of the sinuses. Small pseudo-tubercles are found in the connective tissue, where there may be infiltrations of plasma cells and lymphocytes. If the microfilariae are still alive, eosinophils are few or absent. If the microfilariae have been dead for some time, very large numbers of eosinophils may be present. No neutrophils were found even when acute inflammation had been diagnosed clinically. Dead adult worms are often surrounded by necrotic tissue, walled off by epithelioid cells and giant cells, and this can be easily mistaken for tuberculosis, especially when pseudo-tubercles are found near by, and when the filaria has disintegrated. In such cases the examination of many sections may lead to the finding of remains of the nematodes. The changes described are typical, but not specific for filariasis; they strongly indicate a careful search for the nematodes. [For other descriptions of the histopathology of filariasis, see reference in this *Bulletin*, 1936, v. 33, 592, and MICHAEL below.] *G. Lapage.*

MICHAEL, P. **Filariasis among Navy and Marine Personnel. Report on Laboratory Investigations.** *U.S. Nav. Med. Bull.* 1944, May, v. 42, No. 5, 1059–74, 5 figs.

The author reports his experience with cases of infestation with *Wuchereria bancrofti*, acquired in the Samoan region. He took several thousand blood smears, by day and night, from patients with clinical symptoms and used concentration methods, but found no microfilariae; no other features of diagnostic value were seen in the blood picture. Most of the patients developed symptoms 7–9 months after exposure to infestation. They had chills, mild fever, malaise, nausea, and occasional photophobia; they often noted painful swollen red areas on the extremities, which later involved adjacent lymph nodes, and retrograde or centrifugal lymphangitis might follow. The vast majority had funiculitis with or without epididymitis, orchitis or hydrocele; the highest incidence involved the scrotum, followed by the arms and legs. Most patients had one or more relapses and after each attack the remissions lasted longer and the relapses were of shorter duration [*cf.* FLYNN, below].

The author did skin tests with antigen of *Dirofilaria immitis*, using the technique of DICKSON, HUNTINGTON and EICHHOLD [this *Bulletin*, 1944, v. 41, 303]; 268 out of 307 patients (87·3 per cent.) showed positive immediate and delayed reactions, and all the patients were free from infestation with other nematodes.

The histopathology of the lesions is described in detail. Biopsies were made: 36 of 120 specimens showed living or dead worms, 25 in the peripheral lymphatics and 11 in the lymph nodes [*cf.* FLYNN, below]. The author found that surgical investigation of lesions of the spermatic cord was unwise because complicating relapses followed; but the removal of lymph nodes or lymphatics from the arm was harmless and in some cases apparently beneficial since it removed adult worms full of embryos. Four adult pregnant worms were thus removed.

The author emphasizes the value of serial sections and describes the inflammatory reactions observed in the tissues. Calcification of the worms seemed to begin centrally and involved the cuticle last; this is contrary to the finding of O'CONNOR and HULSE [this *Bulletin*, 1936, v. 33, 592]. Living filariae were found to emerge from the cut surfaces of glands after the latter had been left for many hours in normal saline at 37°C.; this saved the labour of minute dissection.

The author concludes that spontaneous recovery takes place after the departure of the patient from the endemic area. It is doubtful whether the infection causes any decrease in fecundity, but if it occurs it is probably only temporary. As no microfilariae were found in the blood, filariasis is unlikely to become a public health problem in the United States. *G. Lapage.*

FLYNN, P. D. **Filariasis Suspects. Review of Cases Admitted.** *U.S. Nav. Med. Bull.* 1944, May, v. 42, No. 5, 1075–9.

The author examined 125 young healthy white male Marines of a battalion formed and trained in American and British Samoa and Wallis Islands who were suspected to have filariasis. After leaving the Samoan area in December 1942, they lived in the New Hebrides and Russell Islands until they began to be admitted to hospital in March 1943. Military duties had involved close association with the native population.

Eight of the patients showed microfilariae either in their blood or in fluid aspirated from lymph nodes; aspiration was done in five patients only.

The shortest interval between arrival in Samoa and the appearance of the first symptoms among the 8 patients in whom infection was confirmed microscopically was 8 months, while the longest interval was 14 months; for the entire group the shortest interval was 1 month, the longest 15 months, and the average 7·6 months.

All the 59 lymph nodes excised (51 inguinal and 8 epitrochlear) showed evidence of chronic lymphadenitis and 24 were regarded as being probably examples of filariasis; no adult worms were found. None of the patients from whom glands were excised had microfilariae in the blood. *G. Lapage.*

STEWART, M. A. **Filariasis.** *Proc. & Papers 13th Ann. Conference Californian Mosquito Control Ass., 1944, Feb. 28 & 29, Berkeley, Ca.* 6–8.

KNIGHTS, H. T. **Comments on Filariasis.** [Correspondence.] *New Zealand Med. J.* 1944, June, v. 43, No. 235, 153–4.

During a stay of three years in Africa the author was often bitten by *Chrysops*. On the voyage back to New Zealand he had frequent attacks of urticaria; when pain in the chest became associated with these attacks he underwent a clinical examination and a Casoni test for hydatid disease. The test was positive, ++, but serial X-rays and the hydatid complement fixation test gave negative results. At the time of writing the present note, 4 years after leaving the *Chrysops* infested area, he had just observed a filarial worm, *Loa loa*, wriggling under the skin of his forearm. [The author does not mention blood examination or other confirmatory evidence.] *J. F. Corson.*

MAZZOTTI, L. & OSORIO, Maria T. Experimentación sobre pruebas alergicas intracutaneas en el diagnostico de la oncocercosis. [**Experiments on Intracutaneous Allergic Tests in the Diagnosis of Onchocerciasis.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1943, Dec., v. 4, No. 4, 353–7. English summary (3 lines).

The authors made two antigens from *Onchocerca caecutiens* digested out of cysts recently removed. Antigen I was made according to the technique of BOSICEVICH (1938) [no reference is given, but see this *Bulletin*, 1939, v. 36, 847]; Antigen II by the same technique, but with the addition of 1 : 20,000 merthiolate. Antigen I, diluted 1 : 10,000, gave negative results in 31 out of 36 healthy people; in 4 it produced a papule less than 5 mm. in diameter; in one it produced a papule 10 mm. in diameter with slight erythema. Antigen II, diluted 1 : 8,000, produced no reaction with a diameter greater than 5 mm. in 10 healthy people. Both antigens were tested in the onchocerciasis zone of Chiapas, in the same dilutions, on patients with nodules and on others from whom nodules had been removed several times but who had no nodules at the time of the tests, although in all of them biopsy of the skin revealed microfilariae. Antigen I was tried on 40 patients without nodules. In 13 of these it caused erythema and in 7 papules with only slightly marked pseudopodia. Tried on 31 patients with nodules this antigen produced papules with erythema around them in 18 and reactions with pseudopodia in 10. Antigen II was tried on 32

patients without nodules ; of these 14 showed erythema and 5 pseudopodia. Tried on 13 patients with nodules it produced erythema in 4 ; and pseudopodia in 2.

All these were immediate reactions appearing before 15 minutes and disappearing in 20–30 minutes. Taking reactions with a diameter of 5 mm. or more, with or without pseudopodia, as positives, the results showed that, with antigen I, 28 out of 40 patients without nodules and 19 out of 31 patients with nodules, were positive ; with antigen II all were positive. Since the 10 healthy people tested with Antigen II were not enough, 71 patients in a Mexican surgical hospital were tested ; 10 of these were considered positive and 13 per cent. gave false positive results. The different results with this antigen were perhaps due to its higher dilution. The high percentage of false positives in patients without onchocerciasis suggests that the antigens are useless for diagnosis ; the authors think that serological diagnosis is not necessary, because the disease can be diagnosed by clinical signs and by the finding of microfilariae by biopsy. They are continuing their work because of its general interest. *G. Lapage.*

VON HOFE, F. H. **An Improved Method of demonstrating Ova of** *Enterobius vermicularis.* *J. Amer. Med. Ass.* 1944, May 6, v. 125, No. 1, 27–8, 2 figs.

A strip of adhesive scotch tape, three-eighths inch wide, is held over the lower end of a half-inch test tube with the adhesive side outwards, and applied firmly to the anus with side-to side rocking to get a satisfactory smear. It is then applied to a microscope slide. Examination under the microscope often shows three to six ova, sometimes many more, in a single field. *J. F. Corson.*

MAZZOTTI, L. & PASTRANA, A. La investigación de triquinosis en tejidos musculares por el metodo de digestion. [**The Investigation of Trichiniasis in Muscular Tissues by the Digestion Method.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1943, Dec., v. 4, No. 4, 337–42. English summary.

Experience shows, say the authors, that in most instances the number of calcified cysts of *Trichinella* found by the digestion method does not correspond with the number found by examination in a compressorium. The authors investigated the reasons for this. They counted the calcified cysts found in diaphragms by the compression method and then digested the same pieces of diaphragm in artificial gastric juice and counted the cysts in the sediment of the digest. The number of cysts found in the digests was always smaller than that found with the compressorium. When 63 cysts dissected from a diaphragm were put in a Petri dish with gastric juice and watched, the authors observed that 40 had disintegrated in 24 hours. and they counted 5 dead larvae. Of the 23 cysts left, 6 were still identifiable after 96 hours. It is evident, therefore, that calcified cysts can disintegrate relatively easily in artificial gastric juice. This partially explains why no cysts may be found by digestion when they have been found with the compressorium and also the lack of proportion found by some workers between the number of calcified cysts obtained in a small specimen of muscle and the number obtained in a piece fifty or more times as big. When the digest is shaken, the digestion of cysts may be more extensive. The age

and condition of the cysts also probably affects the degree to which they can be digested. This digestion of the cysts helps to explain the discrepancy between the numbers of cysts obtained by compression and those obtained by digestion. An explanation given by other authors is that dead larvae and cysts do not easily pass the screen of the Baermann apparatus used in the digestion method.

The authors think that, for examination by compression, pieces of diaphragm weighing more than 1 gm. should be used. They themselves used pieces weighing 10 gm. They used the digestion method only on those samples which were negative to examination by compression. JACOBS (*J. Wash. Acad. Sci.*, 1938, v. 28, 452) found that 100 diaphragms were negative to routine examination by compression and digestion when pieces weighing 1 gm. were used; but when pieces weighing 10 gm. were examined by compression, 6 per cent. were positive. *G. Lapage.*

DEFICIENCY DISEASES.

BEAN, W. B., SPIES, T. D. & BLANKENHORN, Marion A. **Secondary Pellagra.** *Medicine.* 1944, Feb., v. 23, No. 1, 1–77. [402 refs.]

Pellagra has usually been classified as endemic, alcoholic and secondary. In the endemic class are normally included patients who subsist upon diets that contain insufficient niacin (nicotinic acid) for a normal person. Secondary pellagra occurs when some condition interferes with the orderly processes of nutrition in one of a variety of ways. This review classifies these various factors that may produce secondary pellagra, discussing the previous literature and illustrating the conditions from the experience of the authors.

Dr. Spies and his colleagues have studied 388 cases of secondary pellagra, of whom 146 were seen in two hospitals in Ohio during the period 1930–1939, and the remainder in the Nutrition Clinic at the Hillman Hospital in Birmingham, Alabama, in 1940–1941. The factors responsible for the production of secondary pellagra in the two areas were, in general, similar, although pulmonary disease was more important in Ohio, and malaria in Alabama. Apart from pregnancy and lactation, surgical operations were the most important of the factors that precipitated the disease. Other conditions include diseases of the alimentary canal, disorders of the stomach being particularly important. There is a widespread belief that the stomach produces an intrinsic factor that interacts in some way with niacin. The frequency with which hepatic disease is followed by pellagra suggests that the liver may play some as yet unknown rôle in the metabolism of niacin.

It seems that pellagra appears when the body is unable to make an enzyme that contains niacin. This may arise from insufficient ingestion of niacin, from failure to absorb it (for instance, in severe vomiting or diarrhoea), or from failure to metabolize it in ways as yet unknown. Since the amount of niacin required by the body is proportional to the metabolism, the daily requirement is increased by fevers, neoplasms, parasites and childbearing. All these factors are admirably discussed in the course of the review. The bibliography is full and contains many unfamiliar references; but some of the best work (*e.g.*, by SYDENSTRICKER, D. T. SMITH, and RUFFIN) is omitted.

H. M. Sinclair.

BEAN, W. B., SPIES, T. D. & VILTER, R. W. **Asymmetric Cutaneous Lesions in Pellagra.** *Arch. Dermat. & Syph.* 1944, May, v. 49, No. 5, 335–45, 4 figs. [Refs. in footnotes.]

The normal physiology of the skin is not yet well understood; the smaller quantity of blood needed for local metabolism and the larger portion concerned with the regulation of temperature are two problems needing separate study. The skin lesions in pellagra may show different phases of evolution in different parts of the body at one and the same time, both in ambulatory patients and those confined to bed. Such facts suggest that some local factor plays a part. The authors quote STANNUS [this *Bulletin*, 1937, v. 34, 183]—" The facts in regard to the distribution of the exanthem in pellagra may be stated, in reality, quite simply though they appear to have escaped the observation of most pellagrologists. The exanthem tends to appear in those areas of skin which, in any particular individual, have *undergone certain changes* as the result of the action *in the past* of traumata of various kinds, including solar radiation, exposure to cold, friction, pressure, irritants, etc.", the change being in the skin capillaries, the agent being non-specific.

In view of the suggestion that local factors determine the site of the pellagrous eruption Bean and his colleagures made a study of all their cases exhibiting an asymmetrical distribution of lesions. Among 889 cases of pellagra 32 (3·4 per cent.) exhibited unilateral or asymmetrical dermatitis. Case notes of fifteen patients are given—in five the cutaneous lesions were associated with unilateral varicose veins; in five with unilateral pressure or irritation; in two with infected skin wounds; in one with paralysis, while in two no association was noted. In bed cases lesions occurred about the elbow upon which the patient habitually supported himself, etc. In practically all these cases the site of the unilateral lesion appears to have been determined by previous trauma. It would appear that conditions were present which possibly led to inadequate blood supply and so to anoxia. Using electrically heated pads and a pneumatic tourniquet, the authors therefore attempted to produce pellagrous skin lesions, but only in subjects " who were about to experience a new outbreak of the pellagrous exanthem were we able to produce a lesion identical with the naturally occurring cutaneous changes." The conclusion is that " increased local metabolism in the presence of ischemia may produce a change in the skin of a susceptible pellagrin not to be distinguished morphologically from the dermatitis which is part of the disease as it develops spontaneously in malnourished persons." *H. S. Stannus.*

VERMA, O. P. **Note on the Treatment of Angular Conjunctivitis with Riboflavin.** *Indian Med. Gaz.* 1944, June, v. 79, No. 6, 258–9.

" Cases of angular conjunctivitis were successfully treated by the administration of riboflavin. Before treatment, smears showed numerous Morax-Axenfeld bacilli which disappeared after treatment. In the majority of cases, ocular and other signs of riboflavin deficiency were present."

HAEMATOLOGY.

CANBY, C. B., CARPENTER, G. & ELLMORE, L. F. **Drepanocytosis (Sicklemia) and an apparently Acute Surgical Condition of the Abdomen. Report of their Occurrence in a White Youth, with Laparotomy.** *Arch. Surgery.* 1944, Feb., v. 48, No. 2, 123–5. [19 refs.]

A case of sickle cell anaemia in a Sicilian youth, aged 19, and born in America, is described. The symptoms indicated an acute abdominal condition, possibly torsion of the spleen or volvulus of the small intestine, and laparotomy was done. The spleen was enlarged, covered with fibrin and attached to surrounding structures by older fibrous adhesions; it was removed, the patient recovered from the operation and was discharged from hospital about a fortnight after admission. The immediate post-operative diagnosis was multiple infarcts of the spleen, cause unknown. Some weeks later it was found that he had sicklaemia. The blood of his parents and of two brothers and four sisters was examined, but showed no sickle cells.

The authors give a list of cases of sickle cell anaemia in persons with no evidence of recent negro ancestry; they include a Greek, four Italians, eight Sicilians and three Americans. This is stated to be the first recorded instance where laparotomy has been performed in a Caucasian on account of an acute abdominal syndrome in this disease.

J. F. Corson.

VENOMS AND ANTIVENENES.

BOQUET, P. Sur les propriétés immunologiques du sérum de la vipère commune de France (*Vipera aspis*). [**Immunological Properties of the Serum of** *Vipera aspis.*] *C. R. Soc. Biol.* 1943, Nov., v. 137, No. 21/22, 700–701.

It has long been known that the serum of *V. aspis* will protect against the venom of that snake, and the author has previously shown that it will neutralize the venom as efficiently as the best hyperimmune horse serum. He now states that a mixture of venom and viper serum does not precipitate, but addition of therapeutic antivenene causes precipitation, though addition of normal horse serum or anti-*welchii* serum does not. An antiserum prepared by injecting viper serum into rabbits precipitates both the viper serum and the viper venom, but 4 cc. of this antiserum does not neutralize 1·0 mgm. of venom. It appears, therefore, that the viper serum contains an antitoxin capable of neutralizing the venom, and also antigenic non-toxic substances common to the serum and the venom.

Charles Wilcocks.

BATT, B. E. A. **Two Cases of Snake-Bite.** [Memoranda.] *Brit. Med. J.* 1944, Aug. 5, 181–2.

Two boys, aged 12 and 14 years, were bitten by the same *Vipera berus* and both on the hand. The one first bitten suffered considerably from shock. In both a very early symptom was vomiting and both complained of sore throat. The younger was the first to be bitten and probably received more venom than the second. The first was bitten on

the dorsum of the hand and probably directly into a vein, because on incision " very little blood flowed and it clotted immediately." The child was admitted to hospital two hours after receiving the injury and was treated for shock. Antivenene was obtained and as the patient still complained of sore throat and his arm, shoulder and upper part of the chest were tender and oedematous, 10 cc. of it were injected intramuscularly. Recovery was uneventful.

The second boy was bitten on his little finger. Symptoms, vomiting and sore throat, set in 1½ hours later and the hand became swollen and painful. He was admitted to hospital 4½ hours after being bitten. The site was incised and bled freely and a dressing of potassium permanganate was applied.

[The chief interest of this narrative lies in the treatment adopted and in the author's comments. There is no little doubt and difference of opinion regarding the treatment of snakebite. All, however, are agreed that suction is good. This was promptly done by a companion in the case of the second boy ; no mention of it is made in the case of the first, who was more severely bitten. Incision is usually to be avoided, say many, as it increases the likelihood of secondary infection. It was carried out by a master with his penknife in the first case, at the hospital under anaesthesia in the second. FAIRLEY, on the other hand, favours incision. If permanganate is used it should be injected early, but most recent authorities state that no reliance is to be placed on permanganate. Antivenene to be of any service must be given early and in large doses ; to give 10 cc. only and that 44½ hours after the bite is mere waste of antivenene. The author comments, as if it were unusual, that " in this instance the viper did not discharge all its venom at the first bite." A colubrine snake may do this, but it is safe to say that a viperine never does. A colubrine clings on and bites, a viper gives a quick bite and is off. Finally, the author states : " It proved impossible to procure antivenene through the usual channels." He does not say what channels he tried.] *H. Harold Scott.*

DERMATOLOGY AND FUNGOUS DISEASES.

MOURÃO, B. M. O papel do estreptococo, no pênfigo foliaceo (fogo selvagem). Estudo clinico-bacteriologico. [**The Rôle of Streptococci in *Pemphigus foliaceus* (Wild Fire). A Clinical and Bacteriological Investigation.**] *Mem. Inst. Butantan.* 1943, v. 17, 141–285, 28 figs. & 8 graphs. [83 refs.] English summary.

This monograph is a detailed account of an investigation well planned and carried out with the utmost care. Those interested should study carefully the original, for it is so replete with matter that abstract is far from easy and the whole article would repay translation. It is divided into twelve chapters, of which the first is introductory and the last recapitulatory.

LINDENBERG in 1937, as the result of certain experimental work, came to the conclusion that Fogo selvagem (Pemphigus foliaceus), Duhring's dermatitis herpetiformis and ordinary pemphigus all had the same causal agent, a virus. The present author, while acknowledging that search for a virus as the cause of Pemphigus foliaceus should be continued, is of opinion that a streptococcus plays a part and this study is

a serious attempt to clarify the subject and to determine what part this organism does play. In the second chapter he reviews the literature published by many who have isolated the streptococcus from skin affections; recent views tend to enunciate the following sequel of events: a focal infection with streptococci, spread to the general circulation, localization in the skin, and the production of streptococcal bullae.

The broad scheme of the present study has comprised skin cultures, haemocultures and the bacteriological investigation of tissues and fluids, ante- and post-mortem. The clinical study is based on 160 cases: 36 in the initial stage, 87 of the generalized chronic form, 15 of generalized dermatosis (dystrophic form), 12 of localized dermatosis (formes frustes), 8 in the retrogressive stage and 2 cured cases. The "generalized chronic form" includes those with large bullae, those in an advanced foliaceous state, the pustulo-bullous, hyperpigmented, herpetiform and the papillomatous or verrucose.

Skin culture was made in 53 cases: 21 in the chronic generalized form, 16 in the early stage, 8 of the formes frustes and 8 regressing. Culture was made with the fluid of the bullae and with the crusts. Forty-three had streptococci grown from the lesions; all of those with crusts or with purulent contents gave a growth, but none of those with clear fluid. The crusts gave also growths of *Staphylococcus albus* or *aureus*, a diphtheroid organism and, in one instance, a pneumococcus. Of the patients with generalized dermatitis five gave a growth of *Streptococcus haemolyticus* from turbid fluid in the bullae and two from the clear contents of bullae in the same patients. Of the eight *formes frustes* cases four gave a growth of *Staph. albus* from the crusts, one a *Staph. aureus*; two gave a streptococcus, one of the Beta type and one of the Gamma (inert) type.

Skin cultures were made from four cases of Duhring's disease [says the author, but he gives a table showing five]; *Strept. haemolyticus* was grown from both the clear and the turbid contents of bullae in one patient, the same, together with *Staph. albus*, from the turbid contents of another, and *Staph. aureus* alone from the turbid fluid of a third.

Blood cultures were made on 150 patients: 36 in the early bullous stage, 82 of the chronic generalized form, 15 of the "dystrophic" form, 12 of the *formes frustes*, and 5 in an apparently regressive stage. Nineteen gave growth of streptococcus (12·6 per cent.), five a staphylococcus (3·3), 126 (84) were negative. Fourteen of the 19 positive streptococcus patients died. No streptococcus cases were among those in the early stage; 12 were of the generalized chronic form, five of the dystrophic, and one each of the *formes frustes* and the apparently regressive. Blood cultures were tried in six cases of acute febrile pemphigus and of dermatitis herpetiformis of Duhring. *Streptococcus viridans* was grown from one; the others gave no growth at all.

Post-mortem cultures were made from the heart-blood and the tissues of 24 patients. Streptococci were grown from 23 of these, in four a pure culture; the chief of the others were *Bact. coli* and *Staphylococcus albus* or *aureus*. Streptococci alone or with others in the heart-blood of 17, from the spleen in 18, the liver 11, brain 6, kidneys in 5 (none in pure culture), pericardial fluid three.

Later chapters are concerned with the strains of streptococcus isolated, their microscopical and cultural characteristics, chemical and biological reactions, pathogenicity and serological classification. The organism isolated from cases of pemphigus foliaceus belonged to

the Rosenbach haemolytic Beta type and Lancefield's group A, produced acid in dextrose, laevulose, galactose, mannose, saccharose, maltose, lactose, trehalose, dextrin, starch and salicin ; was virulent on peritoneal injection into rabbits, guineapigs, rats and camondongos (Brazilian house-rat).

There follows a discussion of the rôle of streptococci in skin affections, with abundant quotations from the literature. The main conclusions of the author on the whole subject may be epitomized as follows :—

1. Streptococcal infection plays a large part in pemphigus foliaceus.
2. The organism is a Beta-haemolytic streptococcus of Lancefield's group A.
3. It can be isolated from the heart-blood and organs just after death, but dissemination takes place very soon after death of the body.
4. The plasma of patients contains an anti-fibrinolysin.
5. The seriousness of the cutaneous infection is directly connected with the presence and virulence of this organism.
6. It is not present (nor is any other organism) in the clear fluid of vesicles in an early stage, but is always found in the purulent fluid and crusts.
7. It is not possible yet to affirm that this streptococcus is the primary cause of pemphigus foliaceus.

[See also this *Bulletin*, 1943, v. 40, 487, 488.] *H. Harold Scott.*

KEMPER, J. W. & BLOOM, H. J. **Histoplasmosis : Report of Case.** *J. Oral Surgery.* 1944, Apr., v. 2, 167. [Summary taken from *J. Amer. Med. Ass.* 1944, July 15, v. 125, No. 11, 812.]

A man aged 59 entered the hospital complaining of sores on the tongue and upper lip which had had their onset four months before. The lesions persisted throughout the period of hospitalization. Pharyngeal and laryngeal lesions of a similar character developed with hoarseness and cough. There was remittent septic fever, with excessive fatigue, weakness and loss of weight. All lesions were repeatedly submitted to biopsy. In sections stained by the Giemsa method numerous small yeastlike inclusions were noted, chiefly in the reticuloendothelial cells. They could not be definitely identified. The close resemblance of the disease process to histoplasmosis was considered despite failure to substantiate it. The patient received iodides, bismuth, antimony and stibamine glucoside, in addition to sulfanilamide, sulfathiazole and sulfadiazine in full therapeutic dosage for trial periods. Germicidal and parasiticidal solutions were applied topically. The diet was heavily fortified with iron and vitamin concentrates. Radiation therapy was instituted, 900 roentgens being applied to the lip, face and neck fields. Death from cardiac failure ensued six months after the first admission and ten months after the onset of symptoms. Microscopic postmortem studies revealed Histoplasma capsulatum in the adventitia of the smaller blood vessels in the cortex of the brain and in a few mononuclear phagocytes in the leptomeninges. Histoplasma capsulatum was demonstrated in some mononuclear phagocytes in the granulation tissue of the lingual ulcer. An ulcer at the base of the epiglottis showed an occasional Histoplasma capsulatum organism in plasma cells, lymphocytes and giant cells. Many of the organisms were seen in the lymphocytes, plasma cells and large mononuclear phagocytes in the granulomatous tissue of the laryngeal mucosa. Large mononuclear phagocytes in the red pulp of the spleen contained Histoplasma

capsulatum. The liver showed four bodies resembling Histoplasma capsulatum. Giemsa stained sections of the ureters showed two Histoplasma organisms.

ALBERT, W. B. & ZEIGLER, R. F., Jr. **A Simple, Effective Treatment for Epidermophytosis.** *Southern Med. J.* 1944, June, v. 37, No. 6, 348–9.

The authors have been using the following preparation for some years. Salicylic acid U.S.P. 10 gm., Acetone U.S.P. 33 cc., Glycerol U.S.P. 33 cc., 85 per cent. ethyl alcohol 33 cc. The solution has been used on 50 unselected cases of ringworm, including examples of tinea pedis, tinea cruris and tinea circinata. " The treatment was applied by freely mopping the infected areas, and mopping rather vigorously where foot infections were concerned, for two or three minutes, and then waiting for perhaps five minutes before replacing socks or clothing. Instruction in pertinent foot or body hygiene was given so as to lessen the chances for reinfection. The patients were seen again in from five to seven days and when necessary the treatment was repeated. The results were uniformly successful. Relief from itching was prompt, usually a matter of minutes following the application. More than half the patients were completely healed after one application and all were healed after two or three applications at five to seven-day intervals. There were no cases requiring a fourth treatment." One further quotation is necessary . . . " it has been used by one of us in treating his own frequent infections of ' athlete's foot.' "

[There is little doubt that this lotion is of definite value. WHITFIELD for some years used a similar preparation, consisting of 5 per cent. benzoic acid, 3 per cent. salicylic acid, 25 per cent. acetone, in either rectified spirit or spt. vin. meth. (industrial) ; this did not yield the quick results claimed by Albert and Zeigler. The authors do not refer to any microscopical examinations, do not mention periods of quiescence during sporulation, cold weather, etc., and, by admitting that one of them had had to use the lotion to combat his own frequent attacks of tinea pedis, imply that the method is not perfect.]

Sydney Thomson.

GOTTLIEB, A. **Madura Foot or Mycetoma. Report of Two Cases.** *Western J. of Surgery, Obstet. & Gynecol.* 1944, June, v. 52, No. 6, 264–5, 2 figs.

LEITE, S. Micetomas. [**Mycetoma.**] *Clinica, Hygiene e Hidrologia.* Lisbon. 1943, Oct., v. 9, No. 10, 269–76.

A general account.

MISCELLANEOUS.

MUMFORD, E. P. & MOHR, J. L. **Manual on the Distribution of Communicable Diseases and their Vectors in the Tropics. Pacific Islands Section—Part I.** *Suppl. to Amer. J. Trop. Med.* 1944, May, v. 24, No. 3, 26 pp.

The manual, of which the present section is to form one part, is a wartime outgrowth of the senior author's work in the Pacific Islands

Research project carried on at Stanford University since 1939; publication of the material has been made in response to urgent requests, and revised editions will be issued later. In this part the information is given under headings of diseases, which are themselves classified—diseases of doubtful aetiology, diseases due to viruses and rickettsiae, etc. Under each disease are brief statements of the geographical distribution within the area dealt with, but in Table I a summary of the distribution is given, in which some 90 diseases are related to 20 groups of islands. In sections to be published later there will be discussion of more extensive material, including arthropod vectors. References are not given in the present paper, but are promised when final publication takes place in book form.

The information is given briefly, with little comment. It is full enough to indicate that the authors have tracked down their facts by the laborious process of scrutinizing not only official reports, but many isolated papers in a great number of medical journals throughout the world. An impression of the health conditions of these islands is given, but, although the principal diseases are fairly clearly indicated, the patchiness of recorded distribution of some affections is such that a reader would be unwise to assume that absence of record means absence of disease. This does not apply to malaria and infection with the two forms (periodic and non-periodic) of *Wuchereria bancrofti*, the peculiarities of whose distribution are well known, but it does probably apply to tsutsugamushi fever, cerebrospinal meningitis, lymphogranuloma inguinale, pneumonia, and others. The yaws-syphilis controversy evidently needs study. The reviewer has for a long time held the view that in the Pacific (as in many other tropical areas) there is need for coordinated international standards in the reporting of disease, and of planned research into the problems awaiting solution, many of which, until now, have been studied in too haphazard a fashion. A reading of this paper reinforces that opinion.] *Charles Wilcocks.*

FAUST, E. C. **Disease in the Tropical War Zones.** *Gastroenterology.* 1943, Nov., v. 1, No. 11, 995–1012, 11 figs. [15 refs.]

Professor Faust recognizes 6 main regions of the world in which tropical diseases are found :—the neotropical zone of Central and South America ; the Mediterranean basin ; tropical Africa ; the area from the Sudan to Arabia, Iran, India and Burma ; the Dutch East Indies and northern Australia ; and the area from Malaya to China, Formosa and the Philippines. " Each of the above-outlined zones will be considered *ad seriatim* from the viewpoint of its diseases, with especial reference to their epidemiology, distribution and significance."

In the present paper the author points out the need for information on the prevalent diseases of the areas to which the American forces may be sent, and to supply this geographical background he has constructed a series of 10 maps of the first zone (Central and South America). On these are shown the distribution, and in some cases the intensity, of malaria, amoebiasis, hookworm infection, the fevers of the typhus group, plague, yellow fever, leishmaniasis and Chagas's disease, schistosomiasis, filariasis, and leprosy. A few lines of letterpress amplify the information given by the maps, and certain other diseases are referred to in the text only. The maps are clearly drawn and the markings for the diseases are easy to follow.

From the remark quoted above it seems that the author proposes to deal in the same way with the remaining five regions of the world,

and an editorial comment promises the complete series. When the whole is completed, it will form a very useful basis for a world survey of tropical diseases. *Charles Wilcocks.*

FAUST, E. C. **Disease in the Tropical War Zones. III. The Diseases of the Mediterranean Basin and of Tropical Africa.** *Gastroenterology.* 1944, Jan., v. 2, No. 1, 13–31, figs. 12–22. [18 refs.]

In this paper the author discusses two of his nosographical areas together, namely the Mediterranean Basin and Tropical Africa. [This may be the explanation of the fact that there is no Part II of this series.] The diseases concerned are malaria, typhoid, the dysenteries, helminthiasis, leishmaniasis, fevers of the typhus group, dengue, leprosy and venereal diseases; the distribution is illustrated in a series of 11 maps. For each disease, or group of diseases, a few sentences of explanation or comment are added; these contain no new facts, and the subject matter is familiar to those who have studied tropical diseases. The main value of the paper is in the maps, which give a clearly discerned picture of disease distribution. *Charles Wilcocks.*

SAWYER, W. A. **The Introduction of Tropical Diseases other than Malaria into the United States after the War.** *J. Nat. Malaria Soc.* Tallahassee, Fla. 1944, June, v. 3, No. 2, 115–20.

In this address the author, apart from remarking briefly on the diseases concerned, reviewed the part that could be played in relation to them by the American Society of Tropical Medicine, at a meeting of which the address was delivered. The Society may help by giving advice through its members, many of whom would be engaged in control or cure of the introduced diseases; it could formulate programmes of investigation or control; it could exert influence by prompt publication of papers on the subjects concerned; it could put its influence behind the movement to improve the teaching of tropical medicine.

The various diseases, and the possibilities of their becoming established in the United States, are then briefly discussed.

Charles Wilcocks.

YOUNG, Ruth. **Medicine and Nursing in Ethiopia.** *Lancet.* 1944, June 17, 797–8.

The common diseases of Ethiopia include typhus, relapsing fever, pneumonia, venereal diseases, ulcers, scabies, intestinal helminthiasis, trachoma, malaria and leprosy. Tuberculosis is probably not as prevalent as elsewhere in Africa [but the findings of D'ARCANGELO (*Bulletin of Hygiene*, 1944, v. 19, 597) indicate a fairly heavy incidence], and deficiency diseases do not seem to be common. In the absence of any vital statistics, no morbidity or mortality rates are possible.

The author attempted to gain information on maternal and infant death rates by questioning 122 women; there was a remarkably low incidence of complications during childbirth [but in the absence of any indication of the number of maternal deaths to correspond with this number of surviving mothers, too much reliance should, perhaps, not be placed on this finding]. The author thinks that the absence of professional midwives of the type common in India, and who do so much harm there, is probably responsible for the absence of sepsis. These 122 women reported 353 live births, and of these infants 176 had died and

177 were alive; 109 had probably died during the first year of life. The chief causes of this high rate were probably syphilis, gastro-intestinal troubles and pneumonia. Syphilis is very common, and is also probably the main cause of the high sterility rate.

This state of affairs can be ameliorated only by intensive preventive work and teaching of mothercraft and hygiene. Normal deliveries can be left to nature, leaving available trained persons to deal with other work. But, at present, properly trained nurses do not exist there, though there are women dressers; for this work girls of higher standard of education are needed. The number of public health nurses should, in the author's opinion, be much greater than the numbers serving in hospitals, and public health matters should be taught, not in a school attached to a hospital, but one which is an educational institution in itself. Students should be resident, and the proportion of teachers high. The author refers to the memorandum on nursing education in Africa, by Dr. Janet WELCH [this *Bulletin*, 1931, v. 38, 736]; Ethiopia offers a good field for experiment on the lines advocated in that memorandum.

Charles Wilcocks.

ANIGSTEIN, L. **The White Race and the Tropics: a Post-War Problem.** *Texas Reports on Biol. & Med.* 1944, v. 2, No. 2, 141–52.

MRUGOWSKY, J. Ueber sogenannte neue ansteckende Krankheiten. [**The So-Called New Infectious Diseases.**] *Deut. med. Woch.* 1944, Jan. 21, v. 70, No. 3/4, 24–7. [14 refs.]

In this paper the author expresses a timely criticism of the tendency to regard unfamiliar infectious diseases as being new. He claims to have had considerable experience of the diseases of the region between the Baltic Sea and the Black Sea.

The "new" diseases discussed are: Bessarabia fever (BOENHARDT, 1942) [see this *Bulletin*, 1944, v. 41, 571], Ukranian fever (WESTPHAL, 1943), Reiter's disease (REITER, 1916), and Russian headache fever (SCHULTEN and BROGLIE, 1943).

The three fevers in this list have already been discussed in this *Bulletin*, in which doubts have been expressed regarding the validity of the authors' claims to have discovered new fevers [see this *Bulletin*, 1943, v. 40, 692, 839, 903; 1944, v. 41, 127].

The general conclusions of the author deserve attention by all who are tempted to introduce new names to the existing nomenclature. The chief sources of fallacy mentioned by the author are:—Negative bacteriological and serological findings, and the failure to find a causative agent, do not justify a claim that the disease is a new one. German soldiers in Russia do not react to the special local infections in the same way as the indigenous inhabitants who are likely to have some degree of acquired immunity resulting from previous attacks. Infections caused by the same agent may be extremely variable in their manifestations. Protective inoculation causes a great modification of the clinical picture, so that anomalous attacks of typhoid and paratyphoid fever are of frequent occurrence. The use of place names is condemned as leading to confusion through duplication. A study of the literature and consultation with physicians who have local experience is strongly recommended.

[The observers of the fevers referred to paid little attention to the epidemiological conditions of occurrence of the diseases.]

The author suggests that Bessarabia fever may be one of the protean forms of trench fever or one of the fevers of the typhoid group modified by inoculation, that Ukranian fever may be a form of typhoid or paratyphoid, that Reiter's disease is probably one of the many types of bacillary dysentery, and that the Russian headache fever may belong to the serous-meningitis group, perhaps similar to Swineherds' disease [see *Bulletin of Hygiene,* 1943, v. 18, 703] or to the disease known in Russia as encephalo-meningitis. *John W. D. Megaw.*

LOWE, T. E. **Eosinophilia in Tropical Disease: Experiences at an Australian General Hospital.** *Med. J. Australia.* 1944, May 20, v. 1, No. 21, 453–6, 1 fig.

The author has studied the degree of eosinophilia in men of the Forces returning to Australia after a few months of tropical service. The total examined is too small to afford valid deduction but the findings will be of interest in stimulating to further work on the subject. As control, the average of 100 healthy women showed 145 eosinophiles per cmm., the limit ranging up to 700 [or almost 9 per cent. of a total leucocyte count of 8,000, which few people would regard as within the normal]. One hundred malarial convalescents gave figures ranging between 0 and 1,350, with an average of 250. [This figure, it will be seen, overlaps the normal to more than half and, as no totals are given, the percentage cannot be calculated. Eosinophilia is not noticed in text-book descriptions of the blood changes in malaria and it may be that these were residues of old helminthic infestation unrecognized, but the author stresses the fact that the eosinophiles in the peripheral blood fall some 24–36 hours before the onset of malaria symptoms and increase again after the attack and he regards this eosinophilia as non-specific and similar to what may occur after any acute bacterial infection.]

In patients convalescing from malaria and also infested with *Trichuris trichiura* [there were only 11 of these] the number of eosinophiles ranged between 240 and 1,700 per cmm., with an average of 710, and of 200 similar convalescents infested with hookworms, from 0 to 12,500 with an average of 1,800. [It is well known that in severe cases of ankylostomiasis eosinophiles may disappear altogether.] The highest numbers of eosinophiles were found in patients with *Strongyloides* infestation; there were eight of these and the average was 2,570 per cmm., with limits of 1,100 and 5,300.

A third group the author classifies as "unexplained eosinophilia"; fourteen came within this category and the "minimum average" figure was 1,300 in a total of 9,300 leucocytes (14 per cent.) and the "maximum average" 2,800 in a total of 12,700 (21·8 per cent.). "Tropical eosinophilia" the author rules out "because of the absence of obvious lung involvement and the afebrile course of the illness." He then details as an instance, a case in which "moist adventitiae were consistently at the back of both lungs" and by X-rays "a general increase in the broncho-vascular markings of the lower and middle zones, but this largely disappeared after some weeks." This patient at one time had a total leucocyte count of 32,500 with eosinophiles 22,425 (69 per cent.). Anthelmintic treatment was tried without avail. [In other words, an almost typical case of Loeffler's syndrome or transitory infiltration of the lungs with eosinophilia. Specific treatment of "eosinophilic lung" by means of arsenicals is not mentioned as having

been tried. Further, this condition may be afebrile. See this *Bulletin*, 1941, v. 38, 538; 1944, v. 41, 425, where other references are given.]

H. Harold Scott.

STEIN, H. B. & MILLER, E. **Acute Thrombocytopenic Purpura associated with Haemorrhagic Bullae, with special reference to Onyalai.** *South African J. Med. Sci.* 1943, Feb., v. 8, No. 1, 1–24. [68 refs.]

[This article is important for two reasons: First, because it is a well thought out, clearly presented and fully documented account of an obscure disease; second, because it shows that, contrary to what has been generally believed, onyalai is not confined to the negro races. Consequently, though much of the article covers ground familiar to readers of this *Bulletin*, it merits a fairly full abstract.]

Some of those who have observed cases of onyalai and investigated them pathologically have classed the disease among the purpuras; nevertheless cutaneous purpura has not been noted in onyalai, perhaps because in the black skin the petechiae are not easy to see; on the other hand, the blood-blisters characteristic of onyalai do not find mention in text-books when dealing with acute thrombocytopenic purpura. This last statement calls for some modification, for in certain cases of *secondary* thrombocytopenic purpura, haemorrhagic bullae have been reported, for example by BAMFORTH and ELKINGTON, HUDSON and others after arsenical injections; by HOFFMANN, KAHN and FITZGIBBON, and by MCGOVERN and WRIGHT after sedormid; by HUDSON after intravenous injection of gold; by RATTNER after insect-bite; by RAPPAPORT after food allergy.

The present study is based on 21 patients admitted to the Johannesburg General Hospital during 2¼ years, February 1940–May 1942, with symptoms of thrombocytopenic purpura with haemorrhagic bullae. Nineteen were natives, 14 males, 5 females; one was a male European, 37 years old, and one a Chinese woman of 36 years. The main characteristics of each are given in a table. There is no need to detail the general run of symptoms here because they were quite typical —bleeding from the mucosae and haemorrhagic bullae in the mouth. Purpuric spots were seen in the skin in 17 and may have been present in the other four, but were not definitely visible in the dark skin. In all those studied the coagulation time and prothrombin index were normal and the bleeding-time was increased (Ivy technique); the platelets were low; two patients only had a total over 50,000 per cmm. and several were down to 5,000 or less. The degree of anaemia depended on the severity of the bleeding. The sedimentation rate was increased in 12 out of 15 tested; serum calcium was normal in the few in which this was estimated. Syphilis played no part. Of the 21 cases, six were mild, six moderately severe, three acute with fatal issue from haemorrhage into the brain, three appeared to be aggravated by menstruation; two of these last died, the third refused hospital treatment; three patients were suffering from other diseases in addition, nephritis, typhoid fever, and malaria respectively; of these the two former died.

Of the non-native patients, the European recovered, the Chinese woman died. There was, in the latter, a history of mild bleeding from the gums for a few days several weeks prior to the sudden onset. She had purpuric spots all over the body, haemorrhage from nose and mouth and blood blisters on tongue and palate. The bleeding was ceasing when she was admitted to hospital, so no special treatment was

given, but three days later the temperature rose to 101°F. and bleeding returned, from nose, mouth and urinary tract. She received blood transfusions and citrated blood intramuscularly and gradually the bleeding stopped. Eight days later, in spite of two transfusions, each of 500 cc., in the interval, bleeding again came on from nose, mouth and vagina, and death occurred three weeks after the first admission. [The authors speak of transfusions and intramuscular injections of blood, but do not mention *auto*haemotherapy, which HELMAN found so beneficial—see this *Bulletin*, 1939, v. 36, 158 ; 1940, v. 37, 675].

Aetiology and pathology are discussed, but no conclusion is reached. Treatment by vitamins, by snake venoms, by X-rays, blood transfusions and injections, and splenectomy are considered and the authors conclude :

" . . . onyalai and acute idiopathic thrombocytopenic purpura are similar in very many respects, although . . . the two diseases should still be kept in separate categories. Onyalai is an idiopathic type of acute thrombocytopenic purpura, and until its aetiology is definitely established, we would recommend . . . a trial of splenectomy in those cases where spontaneous remission fails to set in within a week after the administration of blood."

H. Harold Scott.

SUESSKIND, S. **Favism or Bean Disease.** *Harefuah.* Jerusalem. 1944, June 15, v. 26, No. 12. [In Hebrew 227–30. English summary 230].

" Favism, or bean disease, is caused by the eating of broad beans or inhalation of the pollen of their blossom. It is characterized by Hemolysis, with or without Hemoglobinuria, circulatory and digestive disturbances. The disease is seasonal in incidence, cases being seen from the middle of March to the beginning of June, corresponding to the broad bean season in Palestine. While the literature reports a predominance of cases in males, our nine cases were about equally divided between boys and girls. It is a disease chiefly of children with the majority of cases in later infancy or in pre-kindergarten age. All our cases were Sephardic or Oriental, whether this signifies a group susceptibility to the specific agent or special feeding habits can not yet be definitely said. The former appears to be more likely.

" The direct cause is not known ; thought to be a toxin it is now believed to be allergic in character. The course is stormy, but the prognosis is good. None of our cases died ; the mortality as given in the literature may be as high as 8 per cent.

" After a single or repeated blood transfusion—treatment most specific in its effectiveness—blood regeneration is active and recovery with subsequent treatment with iron is rapid and complete."

TURNER, G. G. **The Site for Intramuscular Injection.** [Correspondence.] *Brit. Med. J.* 1944, July 8, 56.

The author draws attention to the occurrence of serious results from injecting drugs into the gluteal region ; they include neuritis and paralysis from injury to the sciatic nerve, and secondary haemorrhage from the gluteal artery. The proper place for intramuscular injection is the outer side of the thigh, the needle being inserted vertically to the surface and the injection being made into the vastus externus muscle just beneath the fascia lata. On this aspect of the thigh injections can

be made at any place from near the top to about 3 inches above the knee. [Medical Officers in the tropics know that intramuscular injections are sometimes given too far back in the buttock and too near the gluteal vessels and nerves and the sciatic nerve, instead of into the anterior superior quadrant; selection of the thigh would avoid these mistakes and give a larger area for repeated injections, but warning should probably be given that only the *outer* side of the thigh may be used.] *J. F. Corson.*

RAJINDAR PAL. **On the Histological Structure of the Midgut of Mosquitoes.** *J. Malaria Inst. of India.* 1943, Dec., v. 5, No. 2, 247–50, 7 figs. on 1 pl.

No histological differences can be detected between the midguts of four species of mosquito examined: *Anopheles culicifacies*, *A. stephensi*, *A. subpictus* and *Culex fatigans*. In all of them the presence of a delicate peritrophic membrane surrounding the gut contents is confirmed. *V. B. Wigglesworth.*

HERMS, W. B. **The Mosquito Vectors in the Pacific Area.** *Proc. & Papers 13th Ann. Conference California Mosquito Control Ass., 1944, Feb. 28 & 29, Berkeley, Ca.* 12–20.

WYNNS, H. L. **The Danger to Civilian Populations on the Pacific Coast from Mosquito-transmitted Infections in Returning Military Personnel.** *Proc. & Papers 13th Ann. Conference California Mosquito Control Ass., 1944, Feb. 28 & 29, Berkeley, Ca.* 22–8.

YOUNG, J. W. **Dermal Myiasis. Report of Three Cases.** *Arch. Dermat. & Syph.* 1944, May, v. 49, No. 5, 309–11.

The paper consists mainly of a useful general account of myiasis in man. A case of "larva migrans" in which a number of larvae of the "bot fly" [species not named] were present is recorded, and two cases due to larvae of *Wohlfahrtia vigil*, all in the United States.
V. B. Wigglesworth.

GOODHUE, L. D. **Insecticidal Aerosols.** *J. Econom. Entom.* 1944, June, v. 37, No. 3, 338–41.

ROBINSON, G. G. **Testing Insecticides on the Argasid Tick,** *Ornithodorus moubata*, **Murray.** *Bull. Entom. Res.* 1944, July, v. 35, Pt. 2, 95–9.

This paper summarizes in tabular form the results of careful laboratory tests on a very long series of organic compounds as insecticides for the tick *Ornithodorus moubata*. None of these is as effective as pyrethrum. Indeed the tick is extremely resistant to most contact insecticides, both sprays and dusts. Certain derivatives of phenol and naphthalene are active as fumigants and might possibly be of use as soil fumigants in the floors of huts. *V. B. Wigglesworth.*

ROY, D. N. & GHOSH, S. M. **The Mechanism of Action of a Contact Insecticide.** *Bull. Entom. Res.* 1944, July, v. 35, Pt. 2, 161–70, 3 figs. [11 refs.]

From studies on the mosquito *Armigeres obturbans*, on blowflies and on lice the authors conclude that pyrethrum passes through the

cuticle so slowly that the insecticide entering by this route is of no importance in killing the insect. After normal spraying, oily droplets are readily seen in and around the tracheae. They conclude that the spiracles afford the chief means of entry for both sprays and dusts; if the spiracles are blocked the action of pyrethrum sprays and dusts is very slow. *V. B. Wigglesworth.*

FUTCHER, P. H., CONSOLAZIO, W. V. & PAGE, N. **Water Balance of Survivors of Shipwreck in Tropical Waters.** *War Medicine.* Chicago. 1944, Apr., v. 5, No. 4, 203–6.

This is a record of a rough "field trial," rather than a critical laboratory study, and nothing new is added. Nineteen volunteers were observed over a period of 96 hours; for 61½ hours they were on inflatable rubber rafts moored in the Gulf of Mexico; for the remainder of the time they were on the deck of an escort vessel travelling between shore and rafts. Nights as well as days were spent on the rafts. All men wore cotton underclothes and cotton flying suits; sometimes the suits were worn open, and on one occasion some men stripped to the waist. Light cotton headgear was worn by most of the subjects. The men rested on the raft and were allowed not more than 500 cc. of water per day—in some cases fresh water, in others demineralized sea water; only 4 men took their full water ration. Tablet emergency rations were issued, each man taking on an average 53 gm. of carbohydrate, 1 gm. of protein and 5 gm. of fat per day; the ration contained only traces of salt. Swimming, or wetting the clothes with sea water was not allowed, but the trousers were usually wet with water shipped on board, and the shirts were often moist with spray. Some men felt chilly at night, but no other subjective impressions are mentioned. It is not stated whether the men sweated or not. During the test, air temperatures varied from 80 to 86°F., with the relative humidity usually 70–80 per cent. The sea temperature was 82–84°F. There was a wind varying from 3 to 18 m.p.h. During the day, the sun was shining; in the second half of the trial, 6 men were protected from the sun by an awning.

From measurements of the body weights at 0, 48, and 96 hours, urine output and fluid intake, the evaporative loss was calculated roughly for each man; weight of food ingested and of stools passed were not included in the balance. On the first day many men vomited, this also was not considered in the balance. As the weights were only measured to ± 50 gm., the inaccuracies thus introduced are probably negligible. In the first 48 hours, the average weight loss per man was 1·66 kilos. per day; the average fluid intake 295 cc., and the average urine loss 670 cc., with an average evaporative loss of 1·25 litres per day; in the second 48 hours the figures were: weight loss 0·845 kilos., fluid intake 330 cc., urine loss 440 cc., and evaporative loss 0·73 litres. The authors suggest that the high evaporative loss in the first half of the trial was due to the previous régime of the men. [The discrepancy appears to be greater than could be explained on those grounds, other factors concerned were probably:—(1) Inaccuracy of weighing. (2) Greater activity on first day. (3) Vomiting, this may well have been greater than the observers realized. (4) Defaecation.] The men under the awning had a lower evaporative loss, by 130 cc., than the rest.

In their comment the authors compare the results of their field trial with similar studies by other workers. They emphasize the effectiveness of wet clothes in cutting down the evaporative loss and recommend

that men shipwrecked in warm seas should keep their clothes moist with sea water. It is unfortunate that they cannot produce stronger evidence for this recommendation than the following :—

Present Test—clothes partially and accidentally wet—
Average evaporation loss, 730 cc.

GAMBLE & BUTLER's experiment—clothes deliberately wet—
Average evaporation loss about the same.

Test on dry land—men working in laboratory—
Average evaporation loss, 880 cc.

This effect has, however, been demonstrated also in well controlled experiments by other workers.

The authors conclude that " as long as exertion is minimal, seasickness is not excessive, clothing is kept moist with sea water, and a light breeze blows, a supply of 500–1,000 cc. of water a day will prevent the occurrence of dehydration in semi-fasting survivors on lifeboats and rafts in the tropics."

[From their own figures 500 cc. of water per day will not prevent dehydration, it will only slow the process up ; while 1,000 cc. is needlessly generous. With a limited stock of water it is important to lay down narrower limits than these for a daily water ration, and the M.R.C. " Guide to the Preservation of Life at Sea after Shipwreck " [*Bulletin of War Medicine*, 1943, v. 3, 463] recommends initially 18 oz. (just over 500 cc.) per day after one waterless day.]

W. S. S. Ladell.

JOHNSON, R. E., PITTS, G. C. & CONSOLAZIO, F. C. **Factors influencing Chloride Concentration in Human Sweat.** *Amer. J. Physiol.* 1944, June 1, v. 141, No. 4, 575–89, 1 fig. [36 refs.]

The authors start with a full summary of the literature since 1911 and summarize the results in a table. They find that all workers agree that the chloride concentration in sweat (1) tends to increase as work is prolonged, (2) varies markedly between individuals, (3) varies in different regions of the body, (4) varies immensely as the supply of drinking water. There is disagreement on the effects of acclimatization, sweat rate, body temperature, salt intake and changes in plasma chloride. Observations on skin temperatures have been scanty.

Two different sets of experiments are recorded by the authors. (1) *Outdoor experiments* :—Sweat was collected for chloride estimations at intervals in long rubber gloves from the hands and forearms of young men marching. The usual precautions were taken to avoid contamination and evaporation. At the time of collection the temperature and humidity of the environment were observed ; and the pulse rate, rectal temperature, and the nude weight (to estimate the sweating rate) of the subjects measured. (2) *Hot room experiments* :—Six men were made to march on a treadmill at $3\frac{1}{2}$ m.p.h. up various grades, at different temperatures and humidities. Sweat was collected from one arm as in the outdoor tests, and skin temperatures were measured, by means of a thermo-junction, on the opposite arm, which was also enclosed in a rubber glove. In addition the same observations were made as in the outdoor subjects, and blood samples were taken for chloride and protein estimations.

Outdoor experiments.—25 experiments were made and 97 sweat samples collected. Two experiments are considered in detail ; in the first of these, one Group (A) received 9 gm. of salt before marching,

the other Group (B) no salt; in the second, B received salt and A none. Both groups excreted sweat containing less chloride in the second experiment, 30m-eq/1 as against 33 for A, and 40m-eq/1 as against 46 for B. The rectal temperatures were lower in the second experiment for both groups and the sweating rate less; dry and wet bulb temperatures were 9°F. less during the second experiment. In the other series of experiments the authors found that the concentration of chloride in the sweat rose consistently both with an increase in rate of sweating, and with an increase in rectal temperatures; the relation between sweat chloride and rectal temperature is plotted graphically for two subjects.

Hot room experiments.—In all the hot room experiments sweat chloride concentrations were consistently higher than those obtained in the outdoor tests, sometimes the concentration was double. The authors suggest that this is because in the open, the chloride in the sweat is already excreted at a minimal concentration. [This is scarcely an explanation of the disturbing and often noted phenomenon; if the concentration in the out-door sweat was not minimal already any further fall would increase the discrepancy. In any case the reason for the discrepancy remains undiscovered.]

When subjects in the hot room drank water equal to two-thirds of their sweat loss, the average results from two subjects showed that:—(1) Sweat chloride increased as the work was prolonged, but the sweat rate diminished. (2) Changes in sweat chloride could be correlated with changes in urine chloride. (3) When water was drunk the rectal and skin temperatures remained lower than when no water was drunk, and the fall in sweat rate with prolongation of work was not so marked.

The effect of drinking 0·2 per cent. saline to equal the water loss was compared on three subjects with the effect of drinking the same amount of fresh water. The results show that, other things being equal, the sweat chloride is lower after drinking saline, and that, though the initial sweat rate is lower, it does not fall off so rapidly during prolonged work. A table gives the results averaged for the three subjects and shows that, at the same period in the experiments, sweating and skin temperatures were the same after either fresh or salt water; the sweat chloride concentrations were 76m-eq/1 after salt, and 96m-eq/1 after water with rectal temperatures 101·1 and 100·8°F. respectively.

Figures are given which show that the sweat chloride is independent of either plasma protein or plasma chloride concentration. And the authors point out that their figures do not support the view that acclimatization, as such, is accompanied by a lowering of the chloride concentration in the sweat, if the samples compared are taken when the rectal temperatures and rates of sweating are as far as possible the same; the apparent decrease in sweat chloride during acclimatization is due to the fact that a man develops a lower rectal temperature and has a lower sweating rate for a given rate of work when acclimatized than when unacclimatized.

The authors' conclusions are that the concentration of chloride in sweat: (*a*) increases as work is prolonged, (*b*) varies markedly between individuals, (*c*) varies inversely as the supply of drinking water, (*d*) decreases during the course of acclimatization, but only as the rectal and skin temperatures decrease, (*e*) increases as the rate of sweating increases, (*f*) varies directly with the body and skin temperatures, (*g*) varies inversely with the intake of salt. In a further analysis they

conclude that ultimately in the individual only 3 factors are concerned: rectal temperatures, skin temperatures, and rate of sweating; in support of this, various series of observations on two subjects are listed:—(1) In this rectal temperature and sweat rate were the same, but skin temperatures were different; (2) The variable was rectal temperature only; (3) The variable was sweat rate only. The list shows a striking correlation between sweat chloride and skin temperatures. [Skin temperatures several degrees above the rectal temperatures and as high as 106·2°F. are somewhat surprising; the air temperatures at which such readings were obtained are not recorded.] An equally good correlation was obtained between sweat chloride and sweat rate, but the correlation of sweat chloride with rectal temperatures was poor; 11 observations, on two subjects, are reported and in four cases a higher rectal temperature was associated with a lower sweat chloride. The authors state that a better correlation is obtained between rectal temperature and sweat chloride if variations in skin temperature and sweat rate are ignored.

Finally the authors draw attention to the importance of individual idiosyncrasy in governing the level of the sweat chloride. They consider that individual differences in the concentration of chloride in the sweat might be correlated with fitness for work in hot environments; but they do not pursue their suggestions.

[It is disappointing that when so many observations were made more actual results are not given. The use of means derived from different experiments and different subjects makes it difficult to evaluate some of the results. Only forearm and hand sweat is considered; in spite of the established fact that the constitution of the sweat varies in different parts of the body, no attempt is made to show whether or not the samples are representative of mixed sweat from the whole body. The correlation of sweat chloride with rectal temperature is not well substantiated by the results shown; no experiments are described in which sweat samples were obtained from subjects as they cooled down. If sweat chloride concentration varies with rectal temperature the sweat chloride should fall, under these circumstances; in a few experiments of this type carried out by the reviewer, the chloride concentration in the sweat did not fall, but continued to rise. One factor, recognized by the authors but given insufficient weight, is the length of time sweating has continued; the longer the subject sweats the greater the chloride concentration in the sweat; this is well shown by the figures quoted for the salt and water comparisons—in both cases after four hours the sweat chloride concentration was raised, but the rectal and skin temperatures were unchanged and the sweat rates diminished.] *W. S. S. Ladell.*

PALMER, H. A. **Case Report of Psychosis following Heat Stroke.** *J. Roy. Army Med. Corps.* 1944, Apr., v. 82, No. 4, 186–9.

CAMBOURNAC, F. J. C. Sôbre a higiene da habitação do Europeu nas regiões inter-tropicais. [**Domestic Hygiene for Europeans in the Tropics.**] *Clinica, Higiene e Hidrologia.* Lisbon. 1943, Oct., v. 9, No. 10, 257–268, 12 figs. [11 refs.]

BOOK REVIEWS.

EDGE, P. G. [Lecturer in the Division of Epidemiology and Vital Statistics, London School of Hygiene and Tropical Medicine (University of London), etc.]. **Vital Statistics and Public Health Work in the Tropics.** Foreword by Major GREENWOOD, D.Sc., F.R.C.P., F.R.S., etc.]. pp. xii+188. 1944. London: Baillière, Tindall & Cox, 7 & 8 Henrietta Street, W.C.2. [12*s.* 6*d.*]

In this book the main preoccupation of the author is not with the mathematical and statistical assessment of figures concerned with disease in the tropics, but rather with the methods of collecting information, which may ensure, so far as is possible, that the data assembled are sufficiently accurate and complete to permit conclusions to be drawn on which sound public health measures may be based. The reviewer once had the privilege of hearing a lecture by Sir Almroth WRIGHT, on the logic of medicine, in which the speaker explained that logical processes are not difficult in themselves, given reliable data, and that the primary business of the medical man was to make sure of his facts. Edge adopts much the same point of view in relation to the tropical countries, and, naturally, lays stress on the British Colonial Empire.

It is, of course, well known that the demography of tropical countries is poor, and that in spite of the powers given by enactments to the governments of these countries, the processes of registration of the peoples are inadequate. Of the many causes of unreliability in the figures which exist the chief are, perhaps, the poor state of education (judged by European standards), the comparatively small provision of civil servants, whose duties are multitudinous, and the endless and unexpected taboos which possess the native mind. It is with such problems, and with the necessity for their solution, that the author deals, with the authority given not only by many years of scrutiny of Colonial Medical Reports (familiar to readers of the *Supplements* to this *Bulletin*), but also by experience gained in the field.

In the early chapters the importance of public health book-keeping, some of the difficulties encountered in the tropics, and the primary requirements of organization are dealt with; methods of counting or estimating the size of populations are detailed and the complexities of birth registration, especially in relation to local beliefs and superstitions, are explained. The author makes a plea for the collection of more complete and reliable records of sickness than are at present available, and discusses the importance of nomenclature in relation to records of disease. He gives a list of 85 titles of diseases which may serve as a basis for the compilation of local lists; these titles are related to those in the International List of Causes of Death.

In the final chapter the author drives home his point that, in post-war reconstruction, population studies will be necessary as a basis for the solution of health problems, and that these must be founded on carefully ascertained facts. Medical officers in tropical countries, and administrators who plan demographic studies, would be well advised to read this book with care; it will save them many mistakes. Many of the students who have passed through the author's hands will welcome this explicit statement of the lessons he inculcated in his lectures, and not a few of those who have sought and acted upon his advice, before commencing field surveys, will corroborate the wisdom of his teaching. *Charles Wilcocks.*

NAUSS, Ralph Welty [B.Sc., M.D., Dr. P.H., etc.]. **Medical Parasitology and Zoology.** Foreword by John C. TORREY, Ph.D., Professor (Emeritus) of Epidemiology, Cornell University Medical College. pp. xix+534, 95 figs. (1 coloured). 1944. London & New York: Medical Book Department of Harper & Brothers, Paul B. Hoeber, Inc. [30*s*.]

From the foreword it is made clear that the object of this book is "The presentation of the essentials of medical parasitology and zoology to the prospective practitioner of medicine." The author, Dr. Nauss, is Assistant Professor of Public Health and Preventive Medicine at Cornell University, and many years of research and teaching in the subject of parasitology have well fitted him for the writing of a text-book intended for the guidance of medical undergraduates. In the foreword and preface it is stated that parasitology is taught to second-year medical students at Cornell in a separate short course of ten sessions of three hours each. Dr. Nauss apparently considers that this period is inadequate for so important a subject, for he states: "Although we have been able to teach in the manner outlined something of the rudiments of these subjects in the thirty hours of class time available, it seems obviously a handicap to both instructor and student to be obliged to do so. A more consistent relative rationing of the students' time devoted to the basic medical sciences would undoubtedly result in the allocation of considerably more time to medical parasitology and closely related medical subjects." Under these circumstances it is obvious that a book such as this, consisting as it does of some 500 pages, must include many references to aspects of parasitology not dealt with in the medical students' short curriculum. The author, however, has endeavoured to avoid this difficulty by segregating that part of the material which it was not possible to present during class sessions into an appendix and glossary, "and thus avoid tempting the student to memorizing it."

The book thus falls into two parts. The first part, consisting of some 350 pages, is devoted to an account of the protozoa, helminths, arthropods, snakes and venomous animals which directly or indirectly adversely affect the health of man. The second part, comprising about 150 pages, contains an appendix dealing with the technique of laboratory examinations, an excellent glossary and a short bibliography. The result, as might be expected from the work of so experienced an author, is a book well written and stimulating to the reader. In the reviewer's opinion, however, it fails to achieve its avowed object of providing a text-book of parasitology suitable for the use of the medical student, for it lacks that accuracy, conciseness and rigid attention to essentials which renders "Blacklock and Southwell" so popular, while it fails to contain the wealth of reliable information which makes larger volumes, such as "Craig and Faust," so valuable as works of reference. Furthermore, brevity is sometimes achieved only at the cost of clearness or by the omission of information which is important for an understanding of the methods recommended for the control of the parasite or its vector, while some of the statements made, although possibly true, are lacking in evidence and are not generally accepted.

The danger of confusion resulting from a determination to achieve brevity is well illustrated in the table on pp. 246–247, which depicts the arthropods concerned in the transmission of disease. In this table

the only arthropod given as a vector of endemic typhus is *Ceratophyllus fasciatus*, although later in the book an account is given of *Trombicula akamushi* as a vector of Japanese river fever, which is stated to be "probably caused by a rickettsia." The cause of Texas fever is given as "*Babesia lipemina*" transmitted by "*Margaropus annulatus*," and no explanation is furnished as to why these obsolete names are used or why a disease of cattle is included in a list of human ailments. *Stomoxys calcitrans* is listed as a possible carrier of relapsing fever. Most puzzling of all, *Cimex* sp. is stated to carry "plague, typhus fever, relapsing fever, kala-azar." It is true that an explanation of this latter statement, and of some other points, is made later in the text (p. 307), but the book is intended for medical students who are apt to interpret the written word as a statement of literal fact. Minor inaccuracies are not uncommon. Thus the statement is made (p. 212) that the oncospheres of *Dipylidium caninum* are ingested from the hair of the dog by flea larvae; of the genus *Culicoides* (p. 277) the larvae are said to be "frequently called 'blood worms' because of their colour"; and on p. 315 is the statement that "the chief medical interest in fleas is their transmission of bubonic and septicemic plague." Such errors are in the nature of 'slips,' but they are nevertheless misleading.

As regards the omission of important relevant information, the following may be quoted as examples. The reviewer has failed to find any reference to the technique to be employed in preparing ordinary thin blood films or to the making and staining of thick films; nor is any account given of mosquito dissection, or of the method to be employed in the preparation of fresh films for the detection of trypanosomes or microfilariae. Yet all these are points of great practical importance to the student. The account of the louse and of louse-borne diseases is disappointing, and, in a book published in 1944, it is surprising to find no mention of modern methods of control and no reference to the value of prophylactic inoculation against fevers of the typhus group. "Equal parts of kerosene and vinegar" are recommended as a means of eradicating the head-louse; and it is stated that "Ordinary laundry" is effective in destroying the eggs of the body-louse, which is described as laying her eggs on fibres of cloth, no mention being made of the fact that she also lays them on the hair of the body and that this represents the chief difficulty in control. A minor omission regarding the vectors of disease is that, although the life-cycles of *Fasciola hepatica*, *Clonorchis sinensis*, *Paragonimus westermannii* and *Fasciolopsis buskii* are described in some detail, neither the name nor the habitats of the respective molluscan hosts are mentioned—an important hiatus when control is being considered. A similar absence of information regarding treatment is sometimes apparent. Thus, although the therapy of malaria is discussed at some length, no reference is made to the use of intramuscular quinine; and the only treatment recommended for scabies is the "Application of sulphur ointment (5 per cent. in lanolin) at intervals of three to four days." Mosquito repellents are discussed but no mention is made of recent discoveries which have proved more successful than those mentioned by the author.

The following extracts, taken only from that section of the book which deals with malaria, may be quoted as examples of the reviewer's criticism that some of the statements made by Dr. Nauss, although possibly true, are lacking in evidence and are not generally accepted. Writing of *Plasmodium malariae* it is stated (p. 98) that "... Shüffner's dots of tertian malaria, or Maurer's dots of subtertian malaria are

rarely present (Ziemann's stippling)." The suggestion here is that Schüffner's dots or Maurer's dots may occur in cells infected with *P. malariae*, but no evidence is brought forward to support this unusual statement. On p. 102 we find *P. ovale* included " Among several malaria plasmodia of less certain or doubtful status reported for man." This classification seems scarcely justifiable, since nowadays *P. ovale* is almost universally regarded as a distinct human species. On p. 109, when writing of the infection of anophelines, the author states that " Other factors which may be of importance in the transmission are the age of the gametocyte, and possibly inherent qualities of the ingested blood, or the condition of the mosquitoes at the time of ingesting gametocyte-infected blood." These factors may be important, but their importance has yet to be demonstrated. The following quotation is the first of three paragraphs describing blackwater fever (p. 117) : " Blackwater fever occurs almost exclusively among Caucasians who have lived in tropical malarious regions for prolonged periods, and who have suffered repeated attacks of malaria. Its etiology is uncertain, but many investigators associate the condition with the previous history of malaria, although plasmodia may be absent or scanty during an attack or in the internal organs after death. Blood hemolysis occurs extensively, numerous casts being found in the renal tubules and hemoglobin in the urine. Some authors attribute the hemolysis to long-continued use of quinine in the treatment or prophylaxis of malaria but blackwater fever also occurs in untreated cases." Few doctors with tropical experience would agree with the use of the words " almost exclusively " ; Indians coming to West Africa seem as prone to blackwater as Europeans, while the present war has shown that many cases of blackwater occur after only a short residence in the tropics. The statement that many investigators associate the condition with a previous history of malaria implies that some do not ; but surely these must be few in number. Again, it seems dangerous to suggest that some authorities attribute blackwater to long-continued use of quinine in the treatment or prophylaxis of malaria ; it would be more generally accepted if phrased " blackwater fever also occurs in cases treated with drugs other than quinine."

Two pages further on (p. 119) Dr. Nauss writes : " The most reliable method for making an accurate diagnosis of malaria fever is by the demonstration of specific plasmodia in the blood or in material obtained by splenic puncture." This statement appears to attach an unwarrantable and dangerous importance to the value of spleen puncture as a means of diagnosing malaria. On the same page occurs the statement : " Recently, however, synthetic substances have been produced which in some respects appear to surpass quinine. These therapeutic agents are plasmochin and atabrin." In writing of the former drug he remarks (p. 122) : " Relapse occurs less often after its use than after the administration of quinine." The reviewer knows of no reliable evidence in support of either of these statements, when used, as they are here, in a general sense. On the same page it is recommended that when gametocytes are present (and presumably gametocytes are present in every case of malaria) plasmochin should be administered. " After the symptoms have been controlled with quinine, it is considered good practice in every case to administer plasmochin in doses of 1/6 grain (0·01 gm.), three times a day, for a period of five or six days, the usual treatment with quinine being continued at the same time." That treatment with plasmochin is sometimes advisable is not denied, but

that every case should be so treated is not in agreement with present ideas. Writing of quinine prophylaxis Dr. Nauss states (p. 126): "The principal objection to its employment in this way is that protracted administration of the drug may induce quinine-fastness of the strain of plasmodia harboured. Thus, the individual will benefit less from its use as a curative agent." Comment such as this, coming from an authoritative source, is bound to prejudice the medical undergraduate against the use of prophylactic quinine, and it should not be made unless supported by good evidence. In this case, so far as the reviewer is aware, no such evidence exists.

Printer's errors are few, but the following have been noted: p. 76, Stevens for Stephens; p. 246, Aganthocheilonema for Acanthocheilonema; p. 287, *Glossinae palpalis* for *Glossina palpalis*; Schüffner is spelled Shüffner throughout.

The book is profusely illustrated and there is an excellent colour plate depicting the malaria parasites. The majority of the illustrations have been borrowed from other writers; for the most part these have been selected with care, but some, notably those of the bed-bug, the louse and *Sarcoptes scabiei*, are either poor in original quality or have suffered in reproduction. The book is finely printed and bound, and a comprehensive index has been provided. The cost in America is not stated, but apparently it is sold in Britain for thirty shillings.

R. M. Gordon.

TAREEV, E. M. [**Clinical Malaria.**] 299 pp. With 37 charts and figs. [In Russian.] 1943. Moscow: State Medical Publications of People's Commissariat of Health U.S.S.R. [12 Roubles].

The author, who is Director of the Clinical Departments of the Central Institute of Malaria and Medical Parasitology in Moscow (former Institute of Tropical Medicine) and of the Third Moscow Medical Institute, has produced a monograph on malaria which provides a systematic account of the pathogenesis, symptomatology, clinical course, diagnosis and treatment of this disease. In accordance with the special prominence given to the clinical aspects of malaria, questions of aetiology and epidemiology, including mosquito control, have been purposely left out of consideration.

An Introduction, dealing with the history and world incidence, is followed by a general account of malarial infection, in Chapter 1, containing a description of the course of the three main types of malaria, with special reference to primary attacks, relapses and protracted forms. Tareev denies the existence of "chronic" malaria and regards all protracted forms as due to reinfection. Further, a clinical classification of malarial infections is given, followed by a detailed account of immunity in this disease, including host-parasite relationships, course and duration of the infection (stated to be on the average one year in subtertian, two years in benign tertian, and from three to five years in quartan malaria), and the mechanism of immunological reactions. The peculiar nature of anti-malarial immunity, as compared with immunity to other acute infectious diseases, and its bearing on chemotherapy and epidemiology are also considered. Chapter 2, entitled "The fundamental clinical triad," is devoted to the changes produced by malaria in the spleen, liver and blood, and to the relevant methods of diagnosis and determination, such as examination of the spleen, splenometry and haematology. There is also a section on changes in metabolism in the course of the disease, with special reference to

lipoids, sugar, the acid-alkali balance, protein content of the plasma, etc. Chapter 3 deals with the effect of malaria upon other organs and tissues, *viz.*, the skin, lungs, cardiovascular system, kidneys, gastro-intestinal tract, nervous system and sense-organs, including the effect of various chemotherapeutic agents upon the last two. Special forms of malarial infection are considered in Chapter 4, in which detailed accounts are given of coma and other pernicious forms of malaria, including a fulminating type of "benign" tertian, the occurrence of which in Russia has recently been brought to notice [see this *Bulletin*, 1943, v. 40, 436, 668]. Blackwater fever and induced malaria are also dealt with in this chapter, while in its concluding section special consideration is given to malaria in pregnant women and in children (including congenital infection). Chapter 5 is on diagnosis and prognosis of malaria: descriptions are given of various diagnostic methods (parasitological, serological and clinical), of the differential diagnosis, on the one hand, from other specific fevers and, on the other, from various forms of splenomegaly (systemic and local). This chapter is concluded by a section on prognosis in malaria; including its economic importance. The last Chapter (6) is devoted to drug prophylaxis and treatment of malaria. The author first describes the chemical composition and mode of action of the various drugs in use, especially of some Russian preparations, such as acriquine (=atebrin, mepacrine) and plasmocide (=rhodoquine); he then goes on to the methods and courses of treatment (prophylactic and therapeutic) with these drugs and with quinine. It is interesting to note that good results have been obtained with a Soviet quinine preparation, known as "Sovchinet," which is extracted from the entire young plants of *Cinchona succirubra*, now cultivated in Transcaucasia.

For many of the examples quoted in the text the author has drawn upon his own observations. There are a few illustrations but unfortunately their value is lost owing to faulty reproduction. There are no references, though—curiously enough—in the preface the author mentions "a list of bibliography at the end of the book," and there is no alphabetical index.

This monograph gives a very complete and up-to-date account of the clinical aspects of malaria, and will no doubt prove to be a useful guide for Russian physicians and malariologists as well as for those of their foreign colleagues who are conversant with the Russian language.

C. A. Hoare.

BOIX BARRIOS, J. Kala-azar infantil. [**Infantile Kala azar.**] Primera Edición. 110 pp., 3 maps & 28 figs. 1943. Madrid: Ediciones Morata.

In 1942 the author published a long article on the subject of infantile kala azar with particular reference to the cases occurring in Spain [this *Bulletin*, 1943, Vol. 40, p. 23]. The little book now under review covers the same ground: in fact, it appears to be largely a reprint of the article in book form. The author has had a considerable experience of the disease in Spain, having had under his own observation 117 of the 507 cases which have been noted in the Province of Castellón. The information given on all aspects of the subject appears to be reliable, so that those who wish to have a clear picture of infantile kala azar in the Mediterranean area cannot do better than procure the author's useful little book.

C. M. Wenyon.

Printed under the authority of HIS MAJESTY'S STATIONERY OFFICE
By The South Essex Recorders, Ltd., Ilford.

(991) Wt. P9/279 11/44 S.E.R. Ltd. Gp. 432.

ALPHABETICAL LIST OF AUTHORS OR SOURCES.

Albert, W. B. & Zeigler, R. F., Jr., 965.
Archivos Internacionales de la Hidatidosis, 949.
de Assumpção, L., 936.
Australian Military Forces, 916.

Bates, M., 936.
Batt, B. E. A., 961.
Bean, W. B., Spies, T. D. & Blankenhorn, M. A., 959.
——, —— & Vilter, R. W., 960.
Béquignon, R. & Viala, C., 911.
Boix Barrios, J., 982.
Boquet, P., 961.
Boyd, J. S. K., 941.
Brunner, M., Altman, I. & Bowman, K., 952.
Bull, U.S. Army Med. Dept., 940.

Canby, C. B., Carpenter, G. & Ellmore, L. F., 961.
Cawston, F. G., 947.
Clark, H. C., 924.
Compton, A., 941.
Conge, M. & Boyer, F., 944.

Denhoff, E. & Piper, B. C., 918.
Devine, J., 930.
Di Prisco, J., 946.

Eagle, H. & Magnuson, H. J., with Musselman, A. D., 942.
Edge, P. G., 977.

Faust, E. C., 966, 967.
Fenton-Russell, D., 921.
Flynn, P. D., 956.
Fulton, J. D., 929.
Futcher, P. H., Consolazio, W. V. & Page, N., 973.

González, E., 931.
Gorgas Memorial Laboratory Annual Report, 924.

Hartz, P. H., 955.
Hitzig, W. M. & Liebesman, A., 943.
von Hofe, F. H. 958.
van Hoof, L., Henrard, C. & Peel, E., 928.

Johnson, F. H. & Schneyer, L., 923.
Johnson, R. E., Pitts, G. C. & Consolazio, F. C., 974.
Jones, T. C. & Maurer, F. D., 937.
Jukov, N. M. & Krasikova, V. I., 917.

Kaiser, M., 911.
Kalandadze, L. P. & Sagatelova, I. S., 916.
Kallat, S., 940.
Kelsey, F. E., Geiling, E. M. K., Oldham, F. K. & Dearborn, E. H., 923.
Kemper, J. W. & Bloom, H. J., 964.
Khodukin, N. I. & Shterngold, E. J., 939.
——, Soshnikova, M. N. & Kevorkova, V. I., 938.
Knights, H. T., 957.
Konj, J. S. & Yakovleva, O. I., 922.
Kubes, V. & Gallia, F., 905.
Kuhlmann, F. & Heinrich, K., 932.

Lépine, P., Levaditi, J. C., Graber, P. & Giuntini, J., 918.
Levinson, S. O., Milzer, A., Shaughnessy, H. J., Neal, J. L. & Oppenheimer, F., 914.
Lowe, T. E., 969.
—— & Lancaster, H. O., 950, 951.

MacFarlane, W. V., 947.
MacGregor, G. A., 949.
Maplestone, P. A., 951.
Mazzotti, L. & Osorio, M. T., 957.
—— & Pastrana, A., 958.
Medical J. Australia, 934.
Michael, P., 956.
Mohsin Ali Abbasi, M., 910.
Mourão, B. M., 962.
Mrugowsky, J., 968.
Mühlens, 934.
Mumford, E. P. & Mohr, J. L., 965.

Nattan-Larrier, L., Ronchèse, A. D. & Steeg, L., 931.
Nauss, R. W., 978.
Neumann, H., 954.

Ottolina, C. & Atencio, M. H., 945.

Palestine, 939.
Peryassú, A. G., 940.
Peterson, O. L., 935.
Phillips, J. W., 910.
Pick, E. P. & Hunter, J., 924.
Price, F. L. & Mayer, R. A., 930.
Puhlmann, H., 919.

Raettig, H., 932.
Rajindar Pal, 972.
Ratcliffe, H. L. & Parkins, Phyllis V., 941.
Remlinger, P. & Bailly, J., 904.
Reniger-Aresheva, M. L., 919.
Ribbands, C. R., 925.
Robinson, G. G., 972.
Rogan, J. M., 921.
Roy, D. N. & Ghosh, S. M., 972.
Roy. Nav. Med. Bull., 953.
Ruiz Sánchez, F., 942.

Sawyer, W. A., 967.
Schiavi, A., 915.
Scott, J. G., 920.
Seiferth, L. B., 933.
Singh, I. & Singh, I., 927.
Spaet, G., 931.
Stein, H. B. & Miller, E., 970.
Steinberg, I. R. & Crivellari, C. A., 918.
Stewart, F. H., 937.
Suesskind, S., 971.

Tareev, E. M., 981.
Torrey, J. C., 978.
Turner, G. G., 971.

Unti, Q., 915.

Verma, O. P., 960.

Wilson, T. E., 926.
Witzberger, C. M. & Cohen, H. G., 942.
Wolman, M., 933.
Wynter-Blyth, M. A., 914.

Young, J. W., 972.
Young, R., 967.

AN
ANNOTATED BIBLIOGRAPHY OF
MEDICAL MYCOLOGY
1943.
Edited by
S. P. WILTSHIRE, M.A., D.Sc.
DIRECTOR, IMPERIAL MYCOLOGICAL INSTITUTE,
in collaboration with
CHARLES WILCOCKS, M.D., M.R.C.P., D.T.M. & H.
ACTING DIRECTOR, BUREAU OF HYGIENE AND TROPICAL DISEASES,
and
J. T. DUNCAN, F.R.C.S., L.R.C.P. (Ire.), D.T.M. & H.
LECTURER IN BACTERIOLOGY, LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE.

Published 1944] [*Price* 5*s.* 0*d. net, post free.*

Orders should be addressed to the Director, Imperial Mycological Institute, Ferry Lane, Kew, Surrey.

'Moogrol' BRAND
Ethyl Esters of Hydnocarpus Oil
(Stabilised with 4 % Creosote)

For the treatment of Leprosy

The addition of creosote to the ethyl esters of Hydnocarpus Oil prevents the formation of irritant oxidation products.

Specify
'Moogrol' with Creosote

BURROUGHS WELLCOME & CO.
(The Wellcome Foundation Ltd.)
LONDON

LIVERPOOL SCHOOL OF TROPICAL MEDICINE

UNIVERSITY OF LIVERPOOL.

Courses of Instruction.

Two courses of instruction (lasting five months) for the Diplomas in Tropical Medicine and Tropical Hygiene are normally given annually. The next courses will commence on a date to be announced later.

Treatment of Patients.

There is a clinical department at the School for all sufferers from diseases contracted in the tropics. Cases needing hospital treatment are admitted to the Tropical Wards (general and private) of the Liverpool Royal Infirmary, which adjoins the School. Special arrangements are made for members of H.M. Government and for members of certain firms who are regular subscribers to the School.